CHAPTER IX

DIGESTIVE SYSTEM

GENERAL OUTLINES OF THE DIGESTIVE TRACT

Anatomical consideration. The human digestive canal is a long muscular tube consisting of the following parts from above downwards—the mouth (guarded by lips and teeth), tongue, pharynx, oesophagus, stomach, small intestine, large intestine, rectum and anal canal. The ducts of the salivary glands open into the mouth. The proximal end of the stomach (i.e., its junction with oesophagus) is guarded by the *cardiac sphincter*. The distal end of the stomach is guarded by the *pyloric sphincter*. The small intestine begins after the pyloric sphincter and consists successively of the following subdivisions: duodenum, jejunum and ileum (Fig. 292). The duodenum

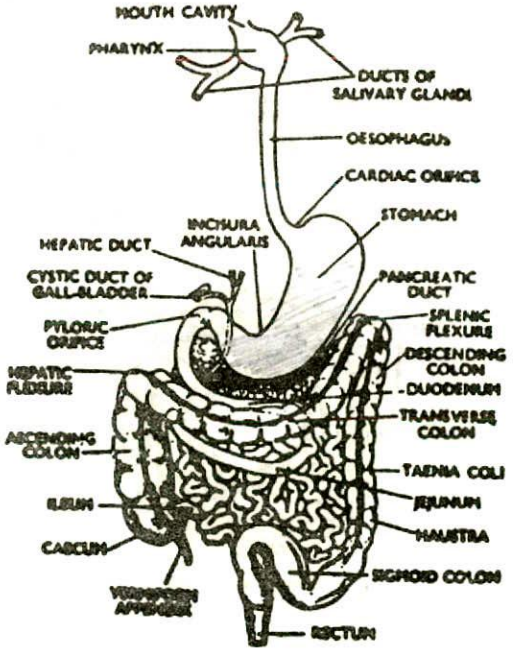


Fig. 292. Diagrammatic representation of the digestive tract showing also ducts of the glands and organs which open into it.

receives food from the stomach. Where the duodenum joins the jejunum, connective tissue and muscle fibres (ligament of Treitz) thicken the mesentery. The bile duct and pancreatic duct jointly open in it through *ampula of Vater*. The small intestine is very long

and is roughly about 7 6 metres (25 feet). The great length of the small intestine provides enough time and surface area, so that digestion and absorption of foodstuff may be complete.

The small intestine opens into the next part—the large intestine. The opening between them is guarded by *iliocolic sphincter*. In the large intestine water is absorbed and the faeces become *formed*. The large intestine opens into the last part—**rectum** and **anal canal**. The latter opens outside through the anal orifice. **Peritoneum** is a serous membrane and lines the interior of the abdominal cavity. The parietal outer layer is in contact with the body wall and the visceral (inner) layer envelops the abdominal organs. **The mesentery** is the continuation of the peritoneum and extends to the small and large intestines from dorsal body wall. The **lesser omentum** of the stomach attaches to the liver and the **greater omentum** hangs from the greater curvature of the stomach over the intestine to the colon as an apron. In this fold fat may accumulate.

Histological structure. The wall of the alimentary canal (Fig. 293) from the oesophagus to the anal canal consists of typical four encircling layers or tunics from outside inwards :

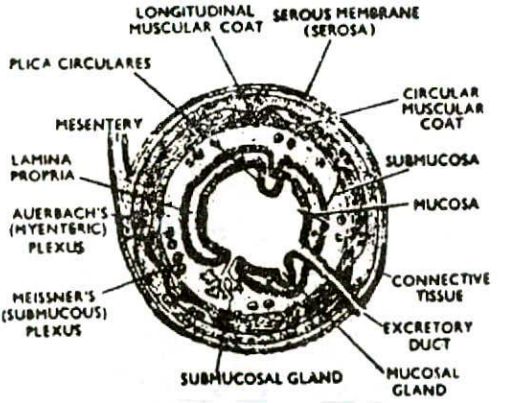


Fig 293. Diagrammatic representation of cross-section of the digestive tract showing the shape of its wall.

1. **Tunica adventitia** or **serosa** (fibrous outer coat) carries large blood **vessels** and nerves. When the organ is covered by the peritoneum, this layer is called **serosa** ; otherwise **tunica adventitia.**

2. **Tunica muscularis** consists of a double layer of smooth muscle of which the inner sheet lies circularly and the outer sheet runs

longitudinally. Nerve and vascular plexuses lie between the layers. This muscular layer controls the diameter of the intestine and propels its contents towards the anus.

3. **Tunica submucosa** is a loose areolar connective tissue layer which contains large blood and lymphatic vessels, nerves and glands in cer ain portions

4. **Tunica mucosa** (mucous membrane) consists of—(*i*) Stratified squamous or single columnar epithelial layer. (*ii*) Lamino propria which is a delicate areolar connective tissue layer and is normally infiltrated with lymphocytes and lymph nodules. (*iii*) Muscularis mucosa is a thin layer of smooth muscle and forms the boundary between mucous membrane and submucosa.

Innervation of the digestive tract. The nerve supply consists of (*i*) an intrinsic part which is represented by nerve cells and fibres originating and located in the intestinal wall itself; and (*ii*) an extrinsic portion which is represented by vagal fibres and postganglionic fibres of the sympathetic. The intrinsic neural structures supply the smooth musculature of the alimentary canal except the striated muscle fibres of the mouth, the upper part of the oesophagus and external anal sphincter. The intrinsic mechanism consists of a

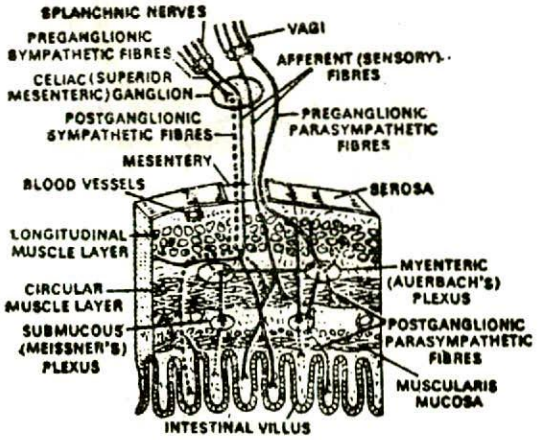


Fig. 294. Diagram showing the cross-section of the intestinal tract with its innervation.

series of plexuses which are composed of large or small groups of nerve cells and bundle of nerve fibres. Two intramural plexuses (Fig. 294) are located in a narrow space (*i*) between longitudinal and

circular muscle layers of the intestinal wall (myenteric plexus of Auerbach) and (*ii*) between circular muscle layer and submucosa (submucous plexus of Meissner). This intrinsic networks of nerves within the walls of the digestive tube is responsible for the spontaneous movements of the intestinal tract even after the extrinsic network has been cut. The extrinsic nerve supply acts to regulate the intrinsic neuromuscular mechanism that determines the movements of the digestive tube. However, the intrinsic neural mechanism is modulated by extrinsic nerves supplied by both divisions of the autonomic nervous system.

The sympathetic fibres which are branches of the splanchnic nerves originating in the celiac (superior mesenteric) ganglion, do not

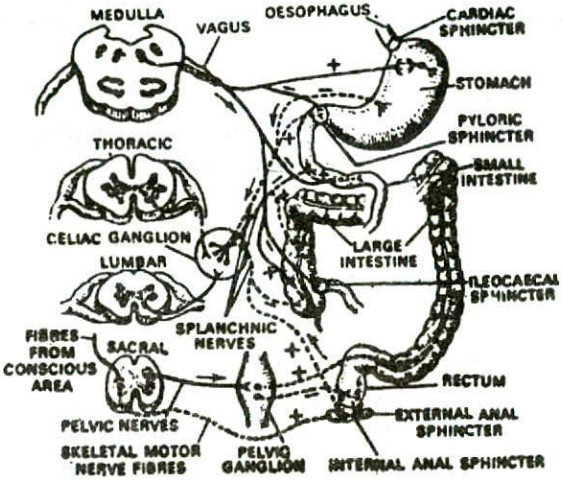


Fig. 295. Diagrammatic representation of innervation of the alimentary canal. *Plus* indicates excitation and *minus*. inhibition.

enter into synaptic junction with the cells of the *intramural* myenteric and submucous plexuses. But they appear to branch in the muscular layers to form intramuscular plexuses and finally to terminate on the smooth muscle fibres. The sympathetic also appear to supply blood vessels within the intestinal wall. The preganglionic parasympathetic fibres are derived from (*a*) the cells in the medulla oblongata and (*b*) the sacral segments of the spinal cord. Those fibres originating from the medulla oblongata are mainly parts of vagal ones and supply muscles of the stomach, small intestine and upper

half of the large intestine. The vagal fibres make synaptic connections with the intramural plexuses. The preganglionic fibres from the sacral spinal cord reach the pelvic ganglion (hypogastric plexus) by way of the plevic nerves and postganglionic fibres supply the lower half of the large intestine and the rectum. The *internal anal sphincter* is innervated by efferent and somatic (motor) nerve fibres. Whereas the *external anal sphincter* is supplied by somatic (motor) nerve fibres (Fig. 295). Although it is difficult to state categorically the results of stimulation of sympathetic and parasympathetic nerve fibres, yet some generalisations can be made. The sympathetic fibres are excitatory for ileocaecal and internal anal sphincters, and smooth muscle fibres of the muscularis mucosa throughout the whole gastro-intestinal canal and help to increase the number of folds in the tract, and are inhibitory for the remaining musculature. The parasympathetic system is excitatory for all the musculature except the sphincters where it is usually inhibitory (Fig. 295). The two nervous systems are antagonistic but so far as *chyme* is concerned, they are compensatory.

Some claim that the intramural plexuses represent complete reflex arcs even though all intestinal neurones are supposedly motor in nature and no local sensory fibres exist. Among two branches of axons of these neurones, one branch receives sensory stimuli and transmits impulse which is generated to the other branch without having to pass through the cell body.

Functions of the digestive system

The human digestive system serves the following functions: (1) **Ingestion** of food. (2) **Digestion** of food. (3) **Secretion** of various digestive juices. (4) **Absorption** of water, salts, vitamins and end products of food digestion. (5) **Excretion**—heavy metals, toxins, certain alkaloids, etc. (6) **Movements**—Certain types of movements are present in the whole of the gastro-intestinal tract. The functions of these movements are to facilitate admixture of food with digestive juices, to propel food onwards, to help blood and lymphatic circulation through the intestinal wall. Defaecation is also due to the movements of the large intestine. (7) **Erythropoiesis**—Stomach manufactures a substance called the intrinsic factor. The extrinsic factor is vitamin B_{12} ; the intrinsic factor interacts with it and helps in the absorption of the extrinsic factor. The extrinsic factor promotes the maturation of the erythroid cells. Pernicious anaemia is associated with *gastric leison.* (8) **Regulates blood reaction** (*vide* under *Blood Reaction*). The alimentary canal takes part in the regulation of blood reaction. (9) **Regulates blood sugar** (*vide* under *Blood Sugar*)—It takes part in the regulation of blood sugar. (10) **Maintains**

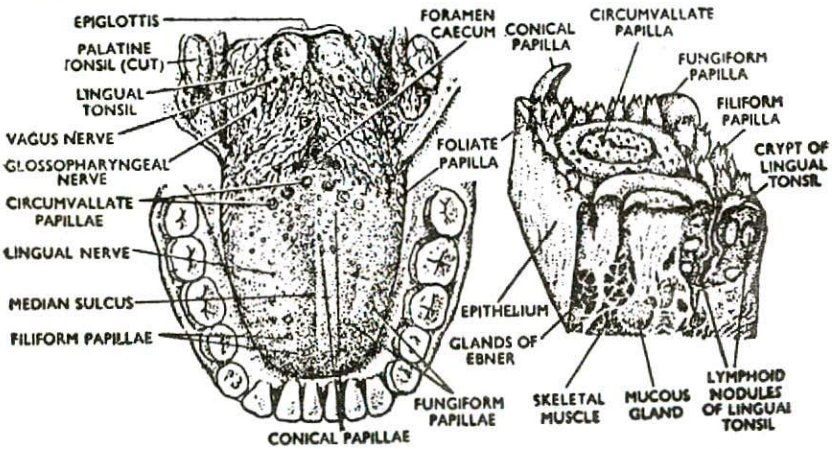
water balance—The phenomenon of *thirst* is an important function of the digestive tract by which the fluid balance of the body is maintained.

The **histological peculiarities of different parts of the digestive canal** are as follows :

Mouth and oral cavity—lined by stratified epithelium.

Tongue

Histology. Tongue (Fig 296) is made up of three elements : *epithelium muscles* and *glands*. The epithelium is stratified and non-cornified. Two types of special structures are seen on it ; the papillae (Fig. 297) and the **taste buds**. The taste buds (Fig. 298) are the sense organs of taste (*vide* under *Special Senses*). These buds are lined by stratified squamous epithelium and are flask-like with a wide bottom. A *taste pore* pierces the short and narrow neck of each taste bud. The taste bud possesses melon-shaped and frequent *supporting* (*sustentacular*) *cells* and also scanty, narrow and long *neuro-epithelial* (*taste*) *cells* to its outer ends. The first are spindle-shaped and their ends surround a small opening, the inner taste pore. The taste cells vary from 4 to 20 per taste bud. They have slender rod-shaped form with a nucleus in the middle, and on the free surface short taste hairs which project freely into the lumen of the pit. These



Fig, 296. Diagrammatic representation of dorsal position of the tongue.

Fig. 297 Diagram shows the structure of papillae of the tongue.

cells are responsible for detection of taste which is to be dissolved in saliva for proper sensation. The papillae are minute projection of the mucous membrane and are as follows : (1) **Circumvallate papillae** are large and can be easily seen with the naked eyes. They are only 10-12 in number situated at the back of the tongue and arranged in

the form of a 'V' with its limbs opening anteriorly. At the apex of the angle there is a small invagination, **foramen caecum.** A *circumvallate* or *vallate* papilla (Fig. 299) consists of a central-rounded elevation, surrounded by the non-cornified stratified squamous epithelium on the lamina propria. External to this groove the mucous membrane is raised and is known as **vallum.** (2) **Fungiform papillae,** having a flat-rounded head like fungus, are covered by the non-keratinising squamous epithelium on the fibrous lamina propria, tip being broader than the base (Fig 301). Circumvallate and fungiform papillae carry taste buds. The fungiform papillae are rich in blood vessels and hence have a marked red colour. (3) **Filiform,** also known as *conical* papillae due to presence of conical pointed cap with keratinising squamous epithelium on the lamina propria (Fig. 300). In man this cap consists

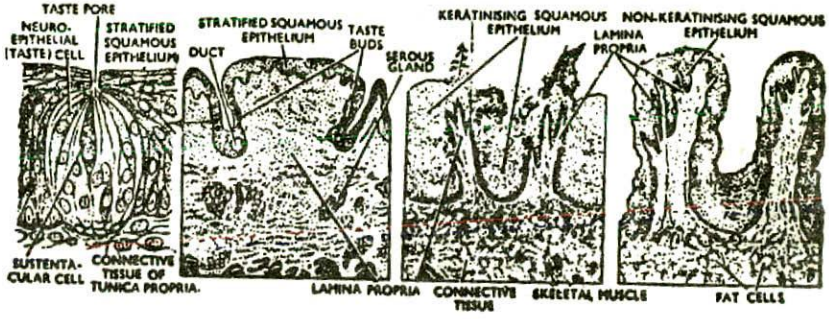


Fig. 298 Fig. 299 Fig. 300 Fig. 301

Histological st uctures of circumvallate, filifrom and fungiform papillae and simplified taste buds (diagrammatic).

of epithelial filaments. (4) **Conical (Conic) papillae,** situated at the dorsum of the tongue, are scattered among the filiform papillae and similar to them, but they are shorter than the filiform. (5) **Foliate papillae,** found on lateral margin of the posterior part, are arranged in several transverse folds. In man they are rudimentary. The filiform and conic papillae possess tactile sensitivity (perceive touch) and all the other papillae gustatory. The muscles of tongue are voluntary and consist of cross-striated muscular fibres.

The glands are small and scattered. They are of three types: **mucous glands, serous glands** and **lymph nodes (glands).** The glands of the last variety are very prominent at the posterior part of the tongue, and are collectively known as the **lingual tonil.**

Nerve supply. The sensation of taste is carried by the *chorda tympanic* branch of the facial nerve (anterior two-thirds of tongue) and the *glossopharyngeal nerve* (posterior one-third). The general sensations of touch, pain, temperature, pressure, etc., are carried by the *trigeminal nerve.* The muscles are supplied by the *hypoglossal nerve.*

Functions. Tongue serves the following functions :

1. **Mastication.** It helps in the act of chewing.
2. **Deglutition.** It helps in the act of swallowing.
3. **Taste**—subserves taste and general sensation.
4. **Speech**—essential for speech.
5. **Secretion** of mucus and of serous fluids with which it keeps the mouth moist.

Salivary glands

There are three pairs of salivary glands **parotid, submaxillary** or **submandibular**, and **sublingual**. One of each pair remains on one side and opens into the oral cavity. The parotid gland opens upon the inner surface of the cheek opposite the second upper molar tooth, by a single duct called the **duct of Stensen**. The submaxillary gland similarly opens by **Wharton's** duct upon the floor of the mouth on the side of the frenulum of the tongue. The sublingual gland, on the other hand, opens by several fine ducts, upon the floor of the mouth by the side of the frenulum. These are called the **ducts of Rivinus** (Fig. 302).

Histologically, salivary glands are typical racemose glands, consisting of lobules which are made up of alveoli and the interlobular septum. Each alveolus is enclosed by a basement membrane upon which the gland cells are arranged. These cells

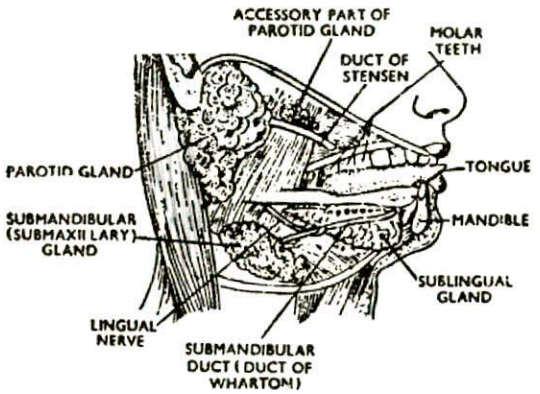


Fig. 302. Anatomical positions of the salivary glands (diagrammatic).

are wedge-shaped, with the thin end of the wedge directed towards the alveoli. Between these cells and the basement membrane, there are a few scattered, flat cells with long cytoplasmic processes. Under electron microscope, myofibrils have been detected in them which lead to the postulation that these cells are contractile, the contraction of which compresses the alveoli and expels its contents into ducts. These cells are known as **myoepithelial basket cells**.

The gland cells may be of two types: *serous* and *mucous*, and accordingly the glands may be of two types. *The parotid gland* (FIGS. 303 & 306) *is composed entirely of serous cells. The sublingual gland* (FIGS. 305 & 308) *is predominantly of the mucous type, whereas submandibular or submaxillary gland* (FIGS. 304 & 307) *is mixed, but in man predominantly of the serous type.* Each **serous cell** has a rounded nucleus towards the base of the cells. There

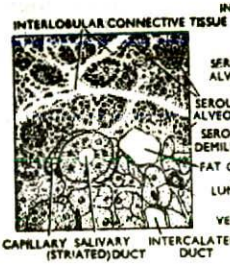


FIG. 303

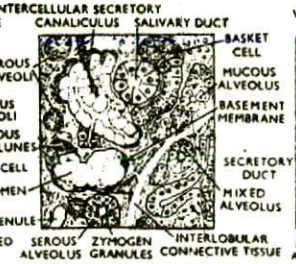


FIG. 304

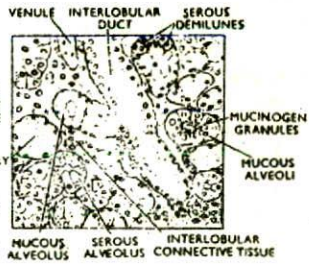


FIG. 305

Histological structures of the parotid, submaxillary (submandibular) and sublingual glands (diagrammatic).

are also chromidial substances which are found to be arranged in parallel lines under the electron microscope. They are probably formed of granules containing ribonucleic acid. In the mixed glands, the serous cells remain compressed at one side of the alveolus in the form of a crescent being sandwiched between the basement membrane and the more numerous mucous cells, lining the alveolus. These crescentic elements are called the **demilunes** or **crescents of Giannuzzi.** The serous cells towards the apices contain numerous fine granules called **zymogen granules** which are more opaque and appear darker in sections than the mucous cells. The **mucous cells** have flattened nuclei towards the base and have got less chromidial substance. These cells contain coarser and less numerous granules called **mucinogen granules.** In addition myoepithelial basket cells described above are present.

The secretion of the serous glands is thin, watery, poor in solid, but rich in enzymes, such as the starch-splitting enzyme, amylase, also known as ptyalin. The secretion of the mucous glands is thick and viscid containing much mucus.

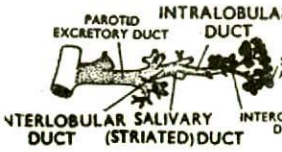


FIG. 306

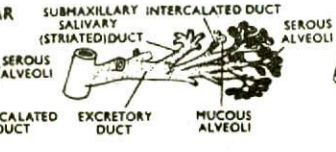


FIG. 307

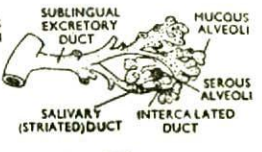


FIG. 308

Diagrammatic representation of structures of parotid, submaxillary and sublingual glands.

The secretion of the glands is conveyed through various salivary ducts. The ducts also modify the composition of the *saliva*. The striated duct cells, which are present in some of the ducts, secrete calcium and iodide into saliva and absorb sodium and water from it. There are *three* types of ducts, e.g., excretory, striated and intercalated ducts composed of four different

types of cells. The **intercalated ducts** lead away from the alveoli and are lined by cuboidal epithelium. The cells are practically filled by large nucleus, cytoplasm is scanty and few if any granules. The **intralobular ducts** are lined by columnar epithelium, which have peculiar rod-shaped appearance. The cells have a centrally placed nucleus and there is a marked striation of the basal one-third of the cell. The **interlobular** or **excretory ducts** are lined by a two-layered epithelium, composed of columnar superficial layer and a flattened deep layer. At the termination the lining of the duct changes to a layered stratified squamous epithelium.

In addition to these three pairs, there are small **accessory buccal glands** scattered throughout the mucous membrane and containing cells chiefly of the mucous type. It has been observed that the histological structure of salivary glands are influenced by **endocrine secretion** of thyroid and sex hormones.

Pharynx or Throat cavity

It is a musculomembrancous tube whose constricted end ends in the oesophagus. Its divisions from above downward are nasal, oral and laryngeal. The mucous membrane lines the pharynx. Its walls are provided with sensory receptors. These receptors are sensitive to mechanical stimulation and are essential in the mechanism of swallowing. When liquid or food stimulates these touch receptors, a complex reflex of swallowing is initiated, but when these sensory areas are anaesthetised, swallowing becomes difficult.

Other than functions of transmission of air from nose or mouth to the larynx and production of voice, pharynx serves as a channel to transport food from mouth to oesophagus. During deglutition or swallowing, closure of mouth and nasopharynx effectively shuts off the pharynx from outside atmosphere. Dilatation of closed pharynx by contraction of pharyngeal muscles results in development of a slight negative pressure. When this effect is combined with thrust, food is pushed downward and onward in the oesophagus. Pharyngeal reflex may be absent in hysteria and glossopharyngeal nerve lesions.

Oesophagus

The mucous membrane of it consists of stratified squamous epithelium. Just under the mucous membrane, there is another very thin layer of plain muscle, called *muscularis mucosae.* Then comes the inconspicuous submucous coat. It consists of collagenous and elastic fibres. Together with the muscularis mucosae, the submucous layer

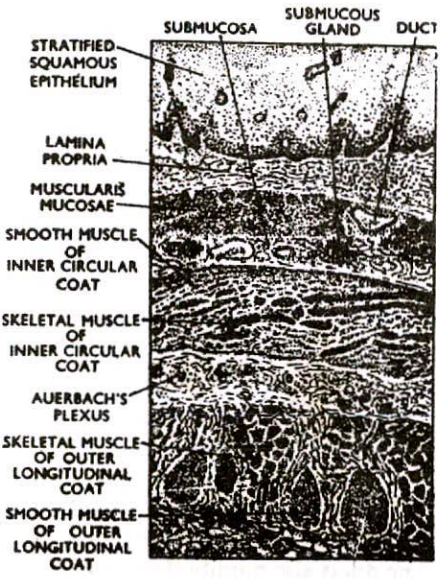


FIG. 309. Transverse representation of upper third of the oesophagus (diagrammatic).

forms numerous longitudinal folds which result in the irregular form of the lumen in cross-section. During swallowing of food, these folds are smoothed out. Outside this, remains the muscular coat consisting of two layers: the outer longitudinal and the inner circular layer. *In the upper third of oesophagus* (FIG. 309) *the muscles are voluntary, in the middle third both voluntary and involuntary, in the lower third only plain muscle is found.* Lastly comes the outermost covering consisting of fibrous tissue, called the **tunica adventitia. Functions**—It receives food from the pharynx and passes it on to the stomach by a series of peristaltic contraction.

Stomach

The shape of the normal stomach is generally like the latter **J.** Sometimes the long axis may be slanting from left to right (*steer horn* type) or it may be even *horizontal.* The junction of the oesophageal mucosa with that of the stomach is abrupt. The oesophago-cardiac line of junction is irregular or zigzag and is often referred to as the **Z** or **ZZ** line. At the pylorus, the mucous membrane of the stomach makes junction with that of the duodenum. The *capacity* of the average stomach is about 1·12–1·70 litres (2–3 pints). It can be subdivided into three parts: the **fundus,** the **body** and the **pylorus,** each of which contains a particular type of gland. The *cardiac area* is the zone, 1 to 4 cm wide that guards the oesophageal orifice, also known as *cardiac sphincter.* The *fundic area* is the largest area of the stomach accounting for 60 to 80% of total mucosal surface, interposed between the cardiac and the pyloric areas. The lower part of

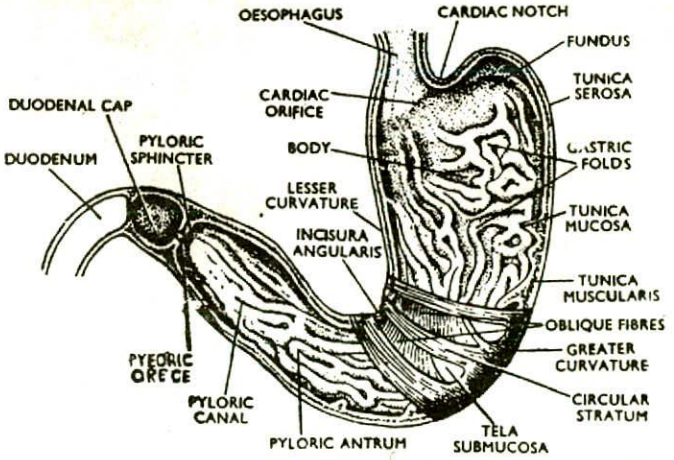


FIG. 310. Diagram represents the frontal section of the stomach and the proximal part of the duodenum.

fundic area is separated from the pylorus by a sharp angle on the lesser curvature; called the **incisura angularis.** The junction of the pyloric and fundic area is not sharply demarcated and is frequently known as the **transitional zone.** The pylorus is limited on the left by the incisura and on the right by the pyloric sphincter. The circular fibres of pyloric sphincter guards against backflow of small intestinal contents into the stomach. The *pyloric area* is about 15 per cent. of the total gastric mucosal area.

It is subdivided into two parts: (*a*) the *pyloric antrum* (pyloric vestibule) which is the short, comparatively wider, proximal chamber, and (*b*) the *pyloric canal* which is the narrow tubular passage, about 3 cm long, ending in the pyloric sphincter (FIG. 310).

Histologically, stomach consists of the same four layers but with certain characteristic differences. The outer serous coat consists of peritoneum. The muscular coat consists of **three layers:** the outer *longitudinal*, the middle *circular* and the inner *oblique* layer. Next comes the submucous coat, then comes the layer of *muscularis mucosae* and a supporting stroma of connective tissue. This layer of muscle also consists of an outer longitudinal and an inner circular layer. Finally comes the mucous membrane which is thrown out into large folds called *rugae* when the stomach is empty and these folds tend to disappear when the stomach is distended. Hence, this folded arrangement of the mucous membrane is a great protective device to prevent damage from stretch. The surface of the gastric mucosa is marked by slight linear depression into small polygonal areas, called **areae gastricae,** giving the surface a mammilated appearance; the areas measure from 1 to 6 mm in diameter. The surface is constantly covered by a thick layer of tough tenacious mucus secreted by the surface epithelial cells, the layer varying in thickness from 0·5 mm to 2·5 mm. Beneath the surface layer of epithelium are located *simple tubular glands* which remain arranged like parallel tubes opening upon the surface. These glands secrete gastric juice. Histologically, as well as functionally, the glands (FIG. 311) are not all same. They differ in different parts of stomach but they are all tubular in structure extending to the muscularis mucosae where they terminate in a blind bulbar end, known as the *fundus* of the gland. The main tubular part is the *body*. The neck of the gland connects the body to the isthmus which communicates with the *gastric crypt*. The total number of glands has been estimated at about 35,000,000.

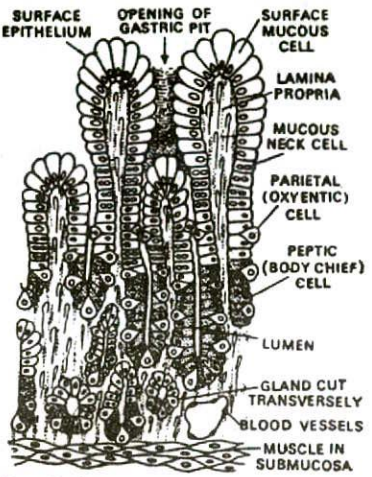


FIG. 311. Diagrammatic representation of tubular glands in the mucosa of the stomach (*body*).

1. **Near the cardiac orifice.** The *cardiac glands* which are short and tortuous are mostly **surface mucous cells** and occupy a small zone around the orifice and secrete mucus although a few pepsinogen cells are also present.

2. **In the fundus and body of stomach.** The fundic glands tend to be straight, slender structures with narrow lumen. The following types of cells are found to compose these glands: (*a*) The **mucous neck cells** –They secrete mucus which is soluble and have been found to constitute part of soluble *mucinogen* droplets of the gastric juice under electron microscope. According to some authors they possibly secrete **intrinsic factor.** (*b*) The **chief (zymogenic) cells** in the *body* of the glands or the

peptic cells—These cells are basophilic and secrete pepsin and contain zymogen granules which are precursors of pepsin. *Histologically*, the cells appear as a typical protein secreting one. In addition to pepsinogen, the chief cells probably produce *gastric rennin*, and a gelatin-splitting enzyme, known as *gelatinase*. (*c*) **Oxyntic (Parietal) cells**—They are found pressed at the bed by chief cells and are oval in shape. They secrete hydrochloric acid (HCl). The cytoplasm of oxyntic cells are stained with acid dyes. Under electron microscope, secretory canaliculi are found to be lined by microvilli from the apical border, deep into cells. (*d*) **Argentaffin (Kulchitsky** or **enterochromaffin) cells**—According to some, a few argentaffin cells, stainable with silver salts and responsible for the secretion of vasoconstrictor *serotonin*, are also present in fundic glands.

3. **In the pyloric region.** Here the glands are fewer in number and shorter in length. They are devoid of both peptic and oxyntic cells. They are entirely lined by cells, resembling the mucous cells, as found in the neck of the fundic glands and secrete alkali and mucus.

The combined secretion of the above glands forms the gastric fluid. High concentration of ribonucleoprotein is present in the enzyme-producing cells. A good number of mitochondria and a Golgi apparatus have been readily demonstrated.

It is to be noted that the secretion of the body and the fundus of the stomach is **acid** *in reaction, and rich in enzyme and chlorides, whereas the secretion of pylorus is* **alkaline** *in reaction, rich in mucus and poor in enzyme and chloride.*

4. **The surface lining** of the stomach consists of *columnar cells* and *goblet cells* (mucus-secreting)

Functions of stomach

1. **Mechanical functions.** (*a*) Stomach receives food material and acts as a *reservoir of food*. (*b*) The movements of stomach help in the proper mixing of food with the digestive juices and also help to propel the food into the duodenum.

2. **Secretion.** Stomach secretes gastric juice which acts as a digestive fluid (Fig. 312). The HCl of gastric juice acts as an antiseptic against swallowed bacteria.

3. **Digestion.** With the help of gastric juice, stomach digests protein up to peptone stage. It also digests fats to some extent with gastric lipase. Gastric rennin coagulates milk. HCl causes some hydrolysis of foodstuffs.

4. **Absorption.** Small quantities of water, saline, alcohol, glucose and certain drugs are absorbed from the stomach.

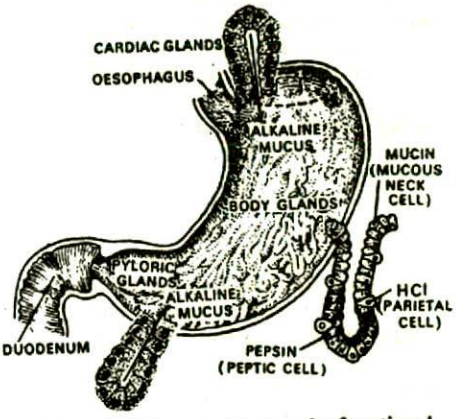


Fig. 312. Diagram showing the functional organisation of the glands of the stomach.

5. **Excretion.** Stomach excretes certain toxins (such as those of uraemia), certain alkaloids like morphine and certain other substances.

6. **Stimulatory functions.** Stomach manufactures two chemical

substances which act as stimulants. They are as follows: (*a*) **Gastrin**—This substance is manufactured by the pyloric mucous membrane and is a true peptide hormone. It acts as a stimulant for gastric secretion. This is responsible for the second phase of gastric secretion. (*b*) **Castle's intrinsic factor**—The normal gastric juice as well as the gastric mucous membrane contains an intrinsic factor. The **extrinsic factor** is vitamin B_{12} taken along with food and the intrinsic factor interacts with it and helps in its absorption. Vitamin B_{12} exerts great influence on the normal development and maturation of red blood cells [*vide* pp. 165–66]. (*c*) There is also **release of enterogastrone** (*enteron, gastron,* chal*one*) from the mucosa of the upper small bowel which *inhibits* gastric secretions.

The **intrinsic factor,** as suggested by Castle, is an enzyme like unidentified substance secreted by the stomach. It is present in the gastric juice as well as in the gastric mucous membrane. The optimum pH for its action is 7 and it is inactivated at temperature above 45°C. It does not necessarily run parallel with the amount of HCl or pepsin in the gastric juice. So that in some cases the intrinsic factor may be present even if there be no HCl or pepsin and *vice versa.* The site of formation of the intrinsic factor varies in different species. In pigs it is obtained from pylorus and beginning of duodenum. In human beings it is present in the fundus and body of the stomach.

7. **Reflex function.** Various reflexes are initiated from the stomach. They are as follows: (*a*) *Gastrosalivary reflex*—Irritation of stomach stimulates salivation. (*b*) *Gastro-ilial reflex*—About half an hour after meal, increased peristaltic movements occur in the last part of ileum. (*c*) *Gastrocolic reflex*—Mass peristalsis is initiated in the colon about half an hour after taking food. (*d*) Presence of food in the stomach *reflexly stimulates pancreatic secretion* and probably also *bile expulsion.*

Small intestine

From outside inwards, the arrangement of the layers is same, i.e., the serous coat, the muscular coat, composed of outer longitudinal and inner circular, the submucous coat the layer of muscularis mucosae consisting of outer longitudinal and inner circular layers and lastly the mucous membrane. The mucous membrane consists of the following three characteristic features: (*a*) The **simple tubular glands** lined by columnar epithelium secrete intestinal juice through the openings between the villi, known as the *crypts of Lieberkuhn.* In much of the small intestine, especially in the jejunum, the mucosa is thrown into the circular folds, called **folds of Kerckring** (Fig. 313). These folds encircle the lumen and serve to increase the surface area of the lumen. (*b*) The **villus** is a slender finger-like fold of the mucous membrane projecting outward from the surface. The surface of the mucous membrane is covered with numerous such projections and the structures of villi

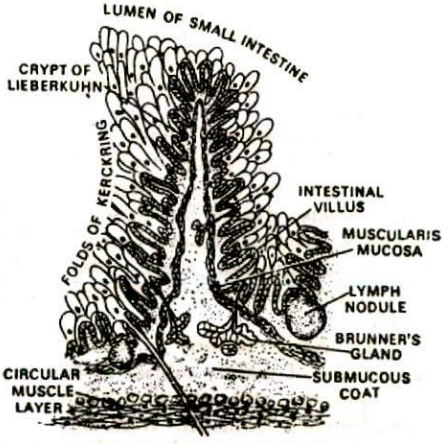


Fig. 313. Diagrammatic representation of a portion of the small intestinal wall showing folds of Kerckring, villi and glands of Brunner.

in the different parts of the small intestine are leaf-shaped in the duodenum, rounded in the jejunum and club-shaped in the ileum. The *function of the villi* is to absorb the different foodstuffs. Their number is about 20–40 per sq. mm. In the jejunum the number is less; in the ileum more. Hence, *the chief function of jejunum is secretion, while that of ileum, absorption.* Each villus consists, at its centre, of a blind lymph vessel called the *lacteal.* It contains a milky fluid rich in fat, hence the name. Outside

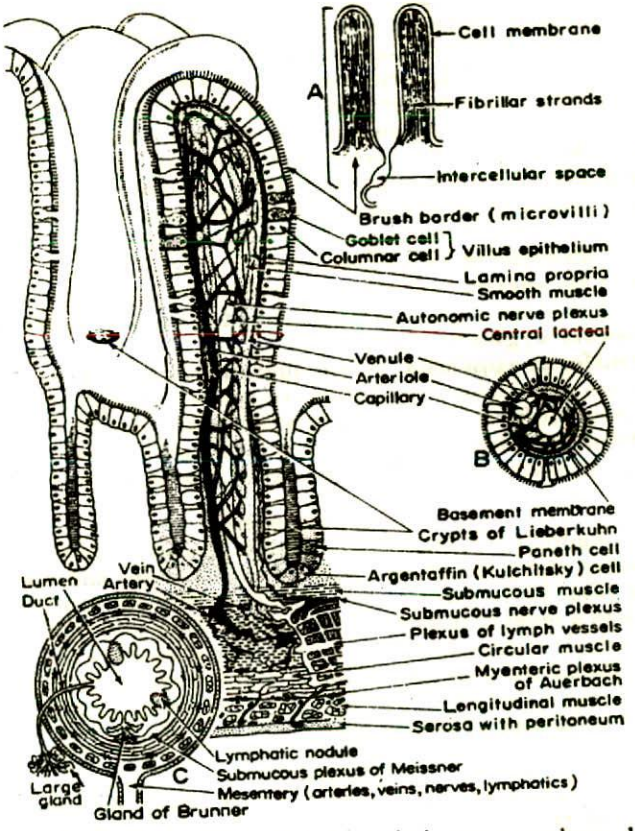


FIG. 314. Diagrammatic representation of intestinal mucous membrane showing the structure of a villus and of adjacent crypts of Lieberkuhn. In inset A, schematic structure of microvilli of the columnar epithelium showing continuity of parent cell membrane and an intercellular space. In inset B, functional organisation in cross-section of the villus showing epithelial cells and basement membrane. Inset C shows cross-section of the intestinal tract.

the lacteal is the loose highly vascular submucous coat. Then comes the superficial mucous layer which is composed of tall columnar epithelial cells and few goblet cells (FIG. 314). The free end of each columnar cell, next to the lumen of the intestine, has a specialised cuticular border, resembling the brush border of certain renal tubular cells. The brush border of the surface epithelial cells of the villi is composed of microvilli

of about 1 μ in length and 0·1 μ in width. The filaments of plain muscles, derived from muscularis mucosae, remain attached to the submucous coat of the villus all round the lacteal. The movements of the villi are due to the contraction of these muscular strips. (*c*) **Lymphoid tissue**—This is another characteristic feature of the mucous membrane. The lymphoid tissue may remain in single isolated forms or in the form of aggregated islands, especially in the ileum, known as **Peyer's patches.**

Here and there among the columnar absorbing cells, are **goblet cells** that secrete mucus. Specialised cells which have the property of reducing ammoniacal silver to metallic silver are called **argentaffin (Kulchitsky) cells.** The cells are found mostly near the base of straight tubular intestinal glands or crypts of Lieberkuhn. The cells are low columnar in shape with nuclei which are larger and clearer than those of neighbouring cells. The cytoplasm contains granules which are always infranuclear in position. Other cells with a large acidophilc nucleus known as **Paneth cells** are found only in the small intestine at the base of crypts of Lieberkuhn and are possibly concerned with the secretion of protein. In addition, there are also found granular **argyrophil cells.**

In the **duodenum,** in addition to these general features, *certain glands are present in the submucous coat under the muscularis mucosae.* These glands open on the surface of the mucous membrane and are called **duodenal digestive (Brunner's) glands.**

Vermiform appendix. It is a blind outgrowth of the caecum which in man is too short to have any functional activity. Lymphoid tissue is very much prominent here, like that of palatine tonsil. Hence, it is sometimes called **abdominal tonsil.** Due to shape it is labile to bacterial invasion and so, inflammation. Surgical removal of this organ is often required.

Large intestine

The longitudinal muscle layer becomes specially collected into three bands passing along the whole length of the large gut and are called the *taeniae coli* (Fig. 292). The circular muscles become thickened at intervals giving rise to a series of pouch-like dilatations. *There is no villus in the mucous membrane* which is thrown into *large folds.* The glands are less in number, lined by *columnar cells* and large number of the mucus-secreting *goblet cells.* In the anal region, the mucous membrane is thrown into longitudinal folds, the **rectal columns of Morgagni.**

Rectum

Histologically, the rectum is similar to the large intestine except that the *taeniae coli* fan out and enclose the tube in an outer longitudinal layer of uniform thickening. The rectum functions as a reservoir for semisolid faeces and rectal valves helps to support the faecal mass as the rectum fills.

Anal canal

This canal is maintained by normal tonus of the puborectalis muscle. In defaecation, the muscular *sling* relaxes and the rectum becomes straight to permit easy passage of stool. The *internal anal sphincter* consists of a thickening of circular layer of smooth muscle. The *external anal sphincter* is a ring of skeletal muscle in an anal triangle.

When the vein becomes varicosed at the junction of the rectum and at the anal canal, *internal and external haemorrhoids* (piles) occur respectively.

The following is a **brief summary of the chief identifying features of different parts of the digestive tract:**

Oesophagus. Stratified epithelium, two layers of muscles which may be voluntary or involuntary, outer fibrous covering.

Stomach. Thick mucous membrane, numerous glands—all of the same height, oxyntic cells, three layers of muscles, outer serous coat.

Small intestine. Villi alternating with crypts of Lieberkuhn, two layers of muscles, serous coat.

Duodenum. Same as above as well as Brunner's glands.

Ileum. Similar as above, presence of Peyer's patches as well.

Jejunum. Absence of either Brunner's glands or Peyer's patches.

Large intestine. Absence of villi, numerous goblet cells, taeniae coli.

DIGESTIVE JUICES

Introduction. There are five digestive juices: **saliva, gastric juice, pancreatic juice, succus entericus (intestinal juice)** and **bile.** The necessity for so many digestive juices is that, (1) one juice does not contain all the enzymes necessary for digesting all the different types of foodstuffs. For instance, saliva contains only carbohydrate-splitting enzymes; whereas gastric juice contains both fat- and protein-splitting enzymes but none acting on carbohydrates. (2) The second reason is that, one particular digestive juice cannot digest a particular type of food up to completion. It will digest only up to a certain stage and then, the products will be handed over to the next digestive juice for further digestion. In this way digestion is completed. For instance, gastric juice digests protein up to the stage of peptone, pancreatic juice carries the digestion of peptone further up to lower peptide. The latter is digested completely up to amino acids by succus entericus.

One more interesting fact about the digestive juices is that, their reactions are not all same. Saliva is slightly acid, gastric juice is strongly acid, but pancreatic juice is strongly alkaline. This, more or less, alternate acid and alkaline reaction, prevents any serious alteration of blood reaction. This is a special device for maintaining blood reaction constant.

The composition and functions of various digestive juices are as follows:

Composition and functions of saliva

Human saliva has the following **characteristics:**

Total amount—1,200–1,500 ml in 24 hours. A large proportion of this 24-hour volume is secreted at meal time, when secretory rate is highest.

Consistency—slightly cloudy, due to the presence of cells and mucin.

Reaction—usually slightly acid (pH 6·02–7·05). On standing or boiling it loses CO_2 and becomes alkaline. This alkaline reaction causes precipitation of salivary constituents, as tartar on the teeth or calculus in salivary duct.

Specific gravity—1·002–1·012. **Freezing point**—0·07–0·34°C.

Composition

Water—99·5%.

Solids—0·5%.

1. **Cellular constituents.** Yeast cells, bacteria, protozoa, polymorphonuclear leucocytes, desquamated epithelial cells, etc.
2. **Inorganic salts**—about 0·2%, consists of NaCl, KCl, acid and alkaline sodium phosphate, $CaCO_3$, calcium phosphate, potassium thiocyanate. Smoker's saliva is rich in thiocyanate. In case of poisoning with metals like lead, mercury, etc., they are secreted in saliva.
3. **Organic**—0·3%.

(*a*) **Enzymes—ptyalin** (salivary amylase) lipase, carbonic anhydrase, phosphatase and a bacteriolytic enzyme, *lysozyme*.

(*b*) Mucin.

(*c*) Urea, amino acids, cholesterol and vitamins (in small amounts).

(*d*) The soluble specific blood group substances also form part of the organic constituents of saliva and they have the same characteristics as the agglutinogen on the erythrocyte. In human beings, the A, B, O and Le^a substances have been demonstrated. Their concentration in saliva is from 10 to 20 mgm per litre.

4. **Gases**—Saliva contains about 1 ml oxygen, 2·5 ml nitrogen and 50 ml of CO_2 per 100 ml.

Bicarbonates, phosphates and the proteins act as buffers. Chlorides activate amylase. The thiocyanate (KCNS) is a product of excretion. It is formed in the body from the cyanogen radicle (—CN) derived from proteins. Its formation is a process of detoxication of the poisonous cyanides and hence is an example of *protective synthesis*. With ferric chloride it gives a rich brown colour.

An enzyme *kallikrein* is present in saliva which acts upon plasma protein to produce a substance known as *kallidin* or *bradykinin*. This produces vasodilatation of salivary gland during secretion and is also responsible for the sudden fall and consequent rise in blood pressure observed after injection of saliva in animals.

Functions

I. **Mechanical functions**

1. It keeps the mouth moist and helps speech. Decrease in salivary secretion as occurs after nervousness, causes impairment of speech.

2. It helps in the process of mastication of the foodstuff and in preparing it into a bolus, suitable for deglutition. Here, saliva also acts as a lubricant.

3. It dilutes hot and irritant substances and thus prevents injury to the mucous membrane.

4. Constant flow of saliva washes down the food debris and thereby does not allow the bacteria to grow. In acute fevers, where the salivary secretion is inhibited, the food debris are not properly washed away and the bacteria multiply. These collect as the *sordes* at the root of the teeth and upon the tongue.

It is to be noted that the mechanical functions of saliva are its chief functions in human beings, and *is mainly contributed by mucin one of its main constituents.*

II. **Digestive functions.** [*Vide* stages of ptyalin digestion under *Digestion of Carbohydrates.*] Saliva contains two enzymes: (*a*) **ptyalin,** which splits starch up to maltose in the following manner:

Boiled starch
↓ *ptyalin*
(Blue colour with iodine) .. .. Soluble starch
↓
(Red colour with iodine) .. .. Erythrodextrin and Maltose
↓
(No colour with iodine) .. .. Achroodextrin and Maltose
↓
(No colour with iodine) .. .. Isomaltose and Maltose

(*b*) **Maltase** (in traces) converts maltose into glucose.

III. **Excretory functions.** Saliva excretes urea, heavy metals (Hg, Pb, Bi, As, etc.), thiocyanates, certain drugs like iodide, etc. Alkaloids, such as morphine, antibiotics, such as penicillin, streptomycin, etc., are also excreted in the saliva. The excretion of ethyl alcohol by the salivary gland has promted the recommendation that such a test should be used for medico-legal purposes. [It also excretes certain virulent micro-organisms, such as the virus of hydrophoboea, acute anterior poliomyelitis, mumps, etc.]

IV. **Helps in the sensation of taste.** Taste is a chemical sensation. Unless the substances be in solution, the taste buds cannot be stimulated. Saliva acts as a solvent and is thus essential for taste.

V. **Helps water balance.** Saliva keeps the mouth moist. When moisture is reduced in the mouth, certain nerve endings at the back of the tongue are stimulated and the sensation of **thirst** arises. When body water is lost (sweating, diarrhoea, etc.)—saliva is reduced and thirst is felt. The subject feels the necessity of drinking water and thus water balance is restored.

VI. **Helps heat loss.** This is mainly found in animals (dog, sheep, etc.). When they become hot or excited more saliva is secreted causing greater heat loss.

VII. **Buffering action.** Mainly bicarbonate and to a lesser extent phosphate and mucin present in saliva act as buffers. There is an increase in bicarbonate concentration during food intake.

VIII. **Bacteriolytic action.** Cell membrane of different varieties of bacteria contains polysaccharides, lysozyme, the enzyme present in the saliva is a polysaccharidase, thus it dissolves the cell wall of many bacteria and finally kills them.

Composition and functions of gastric juice

The average **composition** of human gastric juice is as follows:

Total quantity—about 500–1,000 ml per meal (1,200 ml–1,500 ml per day).
Water—99·45%.
Total solids—0·55%.
Inorganic—0·15% (NaCl, KCl, $CaCl_2$, calcium phosphate, Mag. phosphate, bicarbonate, etc.).
Organic—0·40%.
(*a*) Mucin.
(*b*) Intrinsic factor.
(*c*) **Enzymes:**
(*i*) **Pepsin.**
(*ii*) Other proteolytic enzymes of the gastric juice are: **Cathepsin, Gastricin, Parapepsin I** and **II.**
(*iii*) **Gastric rennin.**
(*iv*) **Gastric lipase.**
(*v*) Other gastric enzymes are present in minute amounts and are: **Lysozyme, Gelatinase, Urease, Carbonic anhydrase.**

Reaction—strongly acid. **Free HCl**—0·4–0·5%.
Total acidity—0·45–0·6%. It includes free HCl, as well as HCl combined with proteins. It also includes other acids, such as lactic acid. As ordinarily examined, the gastric contents show a lower acidity (0·15% to 0·25% HCl), because the HCl is partly neutralised by mucin and other substances.
pH—0·9–1·5.
Specific gravity—1·002–1·004. **Freezing point**—0·59°C.

Functions

1. The enzyme **pepsin,** with HCl, digests proteins up to the stage of peptone.
2. **Rennin** coagulates caseinogen of milk.
3. **Gastric lipase** digests fat to some degree.
4. **HCl** acts as an antiseptic and causes some hydrolysis of all the foodstuffs.
5. **Excretion**—toxins, heavy metals, certain alkaloids, etc., are excreted through gastric juice.

Composition and functions of pancreatic juice

Total quantity, about 500 ml per meal. About 1,500 ml in 24 hours. **Reaction,** alkaline; **specific gravity**—1·010 to 1·030; **pH**—8·0–8·3 (in

dog). **Inorganic constituents**—The distinguishing chemical characteristic is its high bicarbonate content. The principal bases are **sodium** and **potassium.** Small amounts of *calcium, magnesium* and *zinc* are also present. **Organic constituents**—*Enzymes.* The *enzymes* of pancreatic juice are **trypsinogen, chymotrypsinogen, procarboxypeptidase, nucleotidases (ribonuclease** and **desoxyribonuclease), elastase, collagenase, pancreatic lipase, lecithinase, cholesterol esterase** and **amylase.** Its composition varies according to the means used to cause secretion. The following table shows the difference between *secretin juice* and *pilocarpine juice*:

Constituents	Secretin juice from 3 dogs Sp. gr.—1·014	Pilocarpine juice
Alkalinity; number of ml of (N/10) NaOH equal to 10 ml juice	12·7	5·5
Total solid in 100 ml	1·58 gm	6·4 gm
Total proteins in 100 ml	0·5 „	4·8 „
Ash in 100 ml	0·96 „	1·3 „
Chloride in 100 ml	0·30 „	0·27 „
Total nitrogen	—	0·74 „

Functions

1. **Digestive action**—*Vide* stages of digestion in the pancreatic juice under *Digestion of Carbohydrates, Proteins* and *Fats.*

2. **Neutralising action**—It, being alkaline, neutralises almost equal volume of gastric juice.

Characters and composition of succus entericus (intestinal juice)

Intestinal juice, in pure form, is difficult to collect because it is mixed up with bile and pancreatic juice. It can be collected from fistula preparations, such as Thiry fistula, Thiry-Vella modification, Mann-Bollman fistula. The average composition is as follows:

Total quantity—roughly about 1–2 litres in 24 hours. [Accurate measurement is not possible due to the great length of the small intestine.]

Specific gravity—1·010. **Reaction**—faintly acid to faintly alkaline.

pH—varies from 6·3–9·0, average 8·3.

Water—98·5%.

Solids—1·5%.

1. **Inorganic**—0·8% salts of sodium, potassium, calcium and magnesium with that of chloride, bicarbonate and phosphate. The bicarbonate concentration is higher than it is in the blood or interstitial fluids.

2. **Organic**—0·7%.

A. *Activator*—**Enteropeptidase** (previously known as **enterokinase**). It activates trypsinogen into trypsin.

B. *Enzymes*—

1. **Proteolytic**—

(*a*) **Erepsin**—A mixture of enzymes containing dipeptidases (break down dipeptides into amino acids) and amino peptidases (remove terminal amino acid containing free NH_2 group from polypeptides).

(*b*) Several enzymes acting on the different fractions of nucleic acid, such as **nuclease, nucleotidase** and **nucleosidase.**

(*c*) **Arginase**—acts on arginine producing urea and ornithin.

2. **Carbohydrate-splitting**—

(*a*) **Amylase**—found in traces, acts on starch and dextrin.

(*b*) **Sucrase (Invertase)**—digests cane sugar.

(*c*) **Maltase**—acts on maltose.

(*d*) **Isomaltase.**

(*e*) **Lactase**—breaks down lactose.

3. **Fat-splitting—Lipase.**
4. **Other enzymes—Alkaline phosphatase, cholesterol esterase, lecithinase,** etc.

C. **Mucin**

The small intestine does not secrete enzymes in the sense that secretion occurs in the gastric mucosa or in the pancreas. Most of these digestive enzymes are actually intracellular and are present in the juice only because cells desquamate. *Enteropeptidase* and *amylase* are highly soluble and diffusible and are present in the succus entericus. As regards other enzymes they are mostly present in the epithelial cells. Peptidases (erepsin), lactase, maltase, sucrase (invertase) and lipase are found in the intestinal epithelium as well as in the shed cells present in the juice. Proteases, nuclease, phosphatase and arginase are present in the scrapings of the mucous membrane only. These scrapings also show the presence of all the enzymes mentioned above.

From this it can be concluded that the enzymes discussed above digest the foodstuffs in three ways: *First*, the soluble enzymes—enteropeptidase and amylase, freely exert their action on trypsinogen and starch respectively. *Secondly*, the shed cells break down in the succus entericus, set free their insoluble enzymes which digest polypeptides, disaccharides and fats. *Thirdly*, those insoluble enzymes which remain in the intestinal mucosa and found only in the scrapings, exert their actions of the corresponding substrates during their transit through the epithelium, in the course of absorption.

Functions. *Vide* stages of digestion in the succus entericus under *Digestion of Carbohydrates*, *Proteins* and *Fats*.

BILE

Introduction. Bile is both a product of secretion as well as of excretion of the liver. Minute droplets of bile collect inside the tiny vacuoles of the liver cells and are discharged into the bile capillaries through the intracellular canaliculi. The primary bile capillaries start between hepatic cells as blind tubules. They join together repeatedly and form bigger channels and ultimately come out of liver as the right and left hepatic ducts. The two ducts unite and form the *common bile duct*, which enter into the duodenum, through the *ampulla of Vater*. Through the same ampulla also the pancreatic duct opens. From the upper part of the common bile duct commences the *cystic duct*, which ends in the gall-bladder (Fig. 315). *Formation of bile by the liver is an active process. But entry of bile into the duodenum is intermittent and takes place only after meal.* This

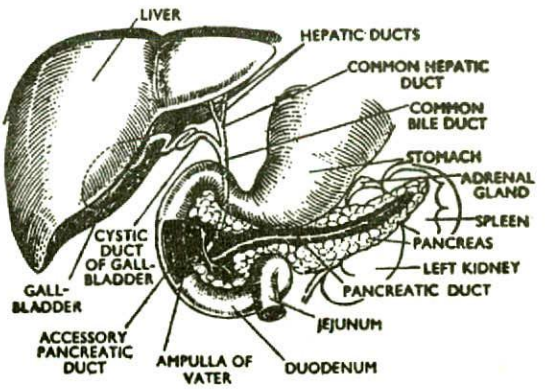


Fig. 315. Schematic representation of the biliary system, pancreas and pancreatic duct.

necessarily indicates that bile must be stored somewhere. Gall-bladder acts as the chief storehouse. The common bile duct also stores some bile.

Composition of bile

Bile is a complex fluid containing various substances, some of which are merely waste products undergoing excretion, whereas others are products of secretion serving important physiological functions. *In the gall-bladder bile is concentrated five to ten times and its alkalinity is reduced* (*vide* 'Gall-bladder'). The composition, as estimated by different observers, varies widely. The usual composition and the characters are as follows:

Total quantity—500–1,000 ml daily. On the average about 700 ml. **Sp. gr.**—1·010–1·011 (Gall-bladder bile—1·026–1·040).

Colour—Human bile is yellowish-green. [In the carnivora, it is golden-yellow, due to the presence of more bilirubin. In herbivora, the colour is green, due to more biliverdin.]

Taste—bitter. **Consistency**—viscid, mucoid liquid. **Reaction**—*liver bile* is definitely alkaline, pH 7·7. [Some hold pH 8·0–8·6.] *Gall-bladder bile* is neutral or slightly alkaline (pH 7·0–7·6) or slightly acid (pH 6·8). That of dog and cat, definitely acid (pH 5·6). **Composition**—total solids, 2–11%. The chief constituents are—(1) **Inorganic salts**—chlorides, carbonates and phosphates of Na, K and Ca and $NaHCO_3$. The total base is equivalent to about 170 ml of (N/10) NaOH per 100 ml of liver bile (300 ml % in gall-bladder bile). (2) **Bile salts**—sodium taurocholate and sodium glycocholate (*vide* page 448). These are the most important constituents of bile and are synthesised by the liver (secretion). (3) **Bile pigments**—of which bilirubin and biliverdin are the chief (*vide* page 449). (4) **Cholesterol, lecithin** and traces of fatty acids, soaps, etc. Cholesterol is probably an excretory product, because its amount in bile varies with its level in blood. It is kept in solution by the hydrotropic action of bile salts. Average composition of human bile is given below (Thorpe).

Constituents	Gall-bladder bile %	Liver bile (bile ducts) %
Water	89·0	98·0
Solids	11·0	2·0
Inorganic salts	0·8	0·75
Bile salts	6·0	0·9
Mucin and Pigments	3·0	0·4
Cholesterol	0·38	0·06
Fats, Fatty acids, etc.	0·82	0·07

Functions of bile

Bile is essential for life. Although it does not contain any enzyme, yet, it acts as a very important digestive juice. Its importance is so much that, life cannot be maintained without it. If a cannula is inserted in the common bile duct and all bile is collected outside, it is seen that the dog develops various abnormalities of bone, anaemia, lack of nutrition and eventually dies (Whipple). Bile serves the following functions:

I. **Digestion.** Bile is essential for the complete digestion of **fats** and to some extent of proteins and carbohydrates. This action is due to the presence of bile salts, which act in the following ways:

(*a*) **By reducing surface tension,** so that fats are converted into an

emulsion. The fine globules of fat, due to their innumerable number, render a larger surface area for the enzyme (lipase) to act. Due to this the process of digestion is quickened.

(*b*) **Activating action.** The bile salts, by virtue of the cholic acid radicle, act as a specific activator for different lipases. [That this action is not due to emulsification is proved by the fact that, although emulsification is unnecessary for the digestion of water-soluble triacetin by pancreatic lipase, yet the action of the enzyme is accelerated by bile salts.]

(*c*) **Solvent action.** Bile acts as a good solvent. Due to this property, it serves as a good medium for the interacting fats and fat-splitting enzymes.

II. **Absorption.** Bile helps in the absorption of various substances. This is also due to presence of bile salts. The following things are absorbed with the help of bile:

(*a*) **Fats.** Bile is essential for fat absorption. This is carried out in two ways: (*i*) **Hydrotropic action**—By this property the insoluble fatty acids, cholesterol, calcium, soaps, etc.,—are made readily soluble in the watery contents of intestinal canal. In this way they are made easily diffusible and thus suitable for absorption. [This action is brought about by the combination of these substances with bile acids. Fatty acids, cholesterol and many such insoluble substances make loose compounds with desoxycholic acid. Such compounds are soluble in water and are called *choleic acids*.] (*ii*) *Bile salts reduce the surface tension of the absorbing epithelium*, increase their permeability and thus facilitate absorption.

(*b*) **Iron, calcium** and probably other mineral constituents of diet.

(*c*) **Vitamins.** Bile salts help in the absorption of lipid-soluble vitamins A, D, E and K; and provitamin *carotene*.

III. **Excretion.** Certain substances are excreted through bile, for instance, (*a*) Some metals like copper, zinc, mercury, etc. (*b*) Toxins, bacteria, etc. (*c*) Bile pigments. [A portion of these pigments is then excreted in the faeces and in urine in various forms.] (*d*) Cholesterol and lecithin are probably chiefly excretory products.

IV. **Laxative action.** Bile salts stimulate peristalsis. When introduced directly into the colon it stimulates peristalsis of these parts.

V. **Cholagogue action.** Bile acts as its own stimulant. Bile salts are the strongest cholagogues. They are absorbed from intestine, carried to liver and stimulate further bile secretion. The taurocholate is stronger in this respect than the glycocholate.

VI. **Bile helps to maintain a suitable pH** of the duodenal contents and thus helps the action of all the enzymes. Bile is an important source of alkali for neutralising the hydrochloric acid entering the intestine from stomach.

VII. **Lecithin and cholesterol,** present in bile, also help in some ways. *First*, they are treated as food and are reabsorbed. *Secondly*, they act as adjuvants to bile salts in the process of emulsification of fats (but on the whole they are regarded as excreted products).

VIII. **Mucin of bile** acts as a buffer and a lubricant.

IX. **Regurgitation of bile** in the stomach helps to neutralise gastric acidity and thus prevents the injurious effect of acids on gastric mucosa.

From the above it will be evident that bile is important not only as a digestive juice but for also various other purposes.

BILE SALTS

Variety and chemistry. In the human bile there are two bile salts almost in equal proportion—(1) **sodium taurocholate** and (2) **sodium glycocholate.** These are the sodium salts of *taurocholic* and *glycocholic* acids respectively.

$C_{23}H_{39}O_5.CO.NH.CH_2.CH_2.SO_3H$ (Taurocholic acid)

$C_{23}H_{39}O_5.CO.NH.CH_2.COOH$ (Glycocholic acid)

Four *bile acids*, cholic acid ($C_{23}H_{39}O_5.COOH$), desoxycholic acid, chenodesoxycholic acid, and lithocholic acid are present in human bile. They are formed from cholesterol, the site of synthesis being liver mitochondrial system. They are also present in the bile in free form. Cholic acid forms soluble compounds with many insoluble substances, such as fatty acids, higher alcohols, etc. Upon this property depends the *hydrotropic action* of bile salts.

Synthesis of bile salts. Site for synthesis—Evidence, accumulated so far, indicates that liver is the site for the synthesis of bile salts. *When bile duct is tied, the bile salts appear in the blood. But when liver is removed no accumulation takes place.* When function of liver is depressed by injury or by the establishment of **Eck's fistula** (Portal vein is connected with inferior vena cava, so that portal blood does not go through liver), the output of bile salts is reduced by 50%. *These evidences show that synthesis of bile salts takes place probably only in the liver.* When cholic acid is administered, along with enough taurine and glycine the concentration of bile salts in the bile increases. With a high protein diet the amount of bile salts increases. With carbohydrate, their concentration is lowered. **Mechanism of synthesis—Glycine** is a simple amino acid which is synthesised in the body. **Taurine** is derived from sulphur-containing amino acid, *cysteine*. **Glycocholic and taurocholic acids** are formed by the combination of glycine and taurine with cholic acid respectively. The reaction is represented as follows: (1) Cholic acid + CoA + ATP ⟶ Cholyl CoA + AMP + PPi. (2) Cholyl CoA + Glycine ⟶ Cholyl glycine conjugate + CoA. The second enzyme similarly catalyses conjugation with taurine forming cholyl taurine conjugate. Because of the alkalinity of bile a major part of the conjugated bile acids forms salts with sodium or potassium, the glycocholates or taurocholates.

Enterohepatic circulation and fate of bile salts. When all bile from the common bile duct is collected by a cannula, it is seen that bile salts given by mouth can be quantitatively recovered from the bile in six hours. From these observations it is clear that bile salts are mostly (80–90%) reabsorbed from the intestine and are re-excreted in the bile. A number of other substances are excreted in the bile along with bile salts and most of them act as **choleretics.** This cyclical migration of the bile salts is called *enterohepatic circulation.* At each cycle a small part is lost in the faeces, which makes about 10–20% of the total amount. Normally, liver synthesises only this lost amount to keep up the usual quantity.

Functions of bile salts

Most of the important functions of bile are due to the presence of bile salts. It will be seen that, as the bile salts run in the enterohepatic circulation, they serve some important functions at each step. The functions may be summarised as follows step by step:

I. **While present in bile** (i.e., in liver and bile channels), bile salts keep insoluble cholesterol in solution (by hydrotropic action). The normal

ratio between cholesterol and bile salts in the bile, varies from 1 : 20 to 1 : 30. When this ratio falls to 1 : 13 cholesterol is precipitated and forms gall-stones (Best and Taylor). Others put the ratio at a much lower figure, viz., 1 : 8, which is actually found to be the ratio between cholesterol and bile acids in samples of bile, containing gall-stones. The ratio in normal bile is usually above this (Thorpe). *Biliary stasis* and *infection of gall-bladder* are the factors contributing the formation of gall-stone.

II. **While present in the intestine** they subserve the following functions: (1) *Digestion of fats* and to some extent of other foodstuffs. This is done in three ways: *First*, by reducing surface tension of water, fat is emulsified, thus rendering larger surface area for the enzymes to act; *secondly*, by activating the lipases directly and thus increasing their actions; and *thirdly*, due to their presence, bile acts as a good solvent for the otherwise insoluble substances, viz., fatty acid and water-insoluble soaps, and in this way, acts as a suitable medium facilitating the interaction between fats and the fat-splitting enzymes. (2) *Absorption of* (*a*) fats and partly other foodstuffs; (*b*) iron, calcium and probably other minerals, and also of (*c*) the fat-soluble vitamins—A, D, E and K; and provitamin carotene. (3) *Increase peristalsis of both* small and large intestine and thus acts as a laxative. (4) (*a*) Impairment of fat digestion results impairment of digestion of other food substances, since fat, covering the food particles, prevents enzymes from attacking them; (*b*) under these conditions, the intestinal bacteria causes much putrefaction and production of gas.

III. **While being reabsorbed from the intestine** they exert *hydrotropic action* upon the insoluble substances and thus help their absorption. The insoluble fatty acid is absorbed as fatty acid bile-salt complex (*choleic acid*).

IV. **While inside the epithelium.** After entering the epithelium, the conjugated compounds break down and the bile salts become free. A part of it goes back to the surface of the epithelium to carry further loads of fat. In this way this part of bile salts remains within the epithelium and moves like a shuttle carrying fresh loads of fatty acids repeatedly. But the main part enters the portal circulation and is carried back to liver.

V. **While back to liver.** The bile salts act as the strongest cholagogues and thus stimulate bile secretion.

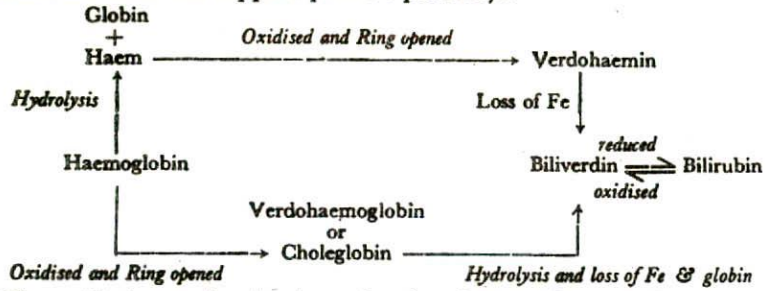
BILE PIGMENTS

Chemistry and varieties. A number of pigments are present in bile. The two chief pigments are **bilirubin** (golden-yellow) and **biliverdin** (green). Bilirubin ($C_{33}H_{36}N_4O_6$) is the chief pigment of human and carnivorous bile. Biliverdin ($C_{33}H_{36}N_4O_8$) is the oxidation product of bilirubin. It is present chiefly in the bile of birds and of herbivorous animals. *Biliprasin* is supposed to be an intermediate product formed during oxidation of bilirubin into biliverdin. *Bilicyanin* (blue), *bilifuscin* (red) and *cholетelin* (yellow) are three other pigments formed by the successive oxidation of biliverdin. They are found in the gall-stones. The bile pigments are porphyrin compounds and constitute about 15–20% of the total solids of the liver bile. [They can be detected by *Gmelin's test.*]

Origin and formation. The old and worn-out red blood cells disintegrate and are removed from the circulation by the cells of the reticulo-endothelial system, the bone-marrow appears to be the most active site. Haemoglobin is released and by degradation, opening of the *porphyrin ring system* occurs. The degraded compound is known as **verdohaemoglobin**

or **choleglobin.** In the next stage it is broken down into *protein* and *haem*. Protein is broken down into amino acids which enter the general *amino acid pool* of the body. The iron present in the haem remains stored in the body as *apoferritin, ferritin* and *haemosiderin* which help in the formation of *new* haemoglobin. The *rest* of the haem is converted into *yellow* pigment bilirubin which is oxidised into *green* pigment biliverdin or the *green* pigment biliverdin is formed first which by reduction forms the yellow pigment bilirubin. *Biliverdin reductase* is the enzyme which catalyses the reduction of biliverdin to bilirubin. These are also derived to some extent from myohaemoglobin.

A schematic representation of bile pigment formation is given below. It does not represent proved steps of the reactions, but only attempts to summarise the facts and supplies possible pathways.



The oxidation and reduction take place by transference of hydrogen from the substrate and NAD/NADH or NADP/NADPH system. The bilirubin then probably combines with albumin of the plasma. When it enters the liver cells, plasma albumin is separated from bilirubin. In the liver cells and to lesser extent in kidney cells it is conjugated with glucuronic acid (UDP glucuronic acid) and forms monoglucuronide and diglucuronide. In hepatic bile these are bound in addition with protein and in gallbladder bile with lipoprotein, cholesterol and bile acids. The reaction is catalised by **glucuronyl transferase.** Some bilirubin is also esterified by sulphuric acid as *bilirubin sulphate.*

Site of formation, circulation and fate. Liver (Kupffer cells), spleen and bone-marrow, being the chief seats of the reticulo-endothelial system, take the main part in bilirubin formation. Blood leaving the spleen and bone-marrow has a much higher bilirubin content than the arterial blood. Normal blood serum contains traces of bilirubin which on the average amounts to about **0·5-0·8 unit.*** It is to be noted that bilirubin, as it is present in blood (haemobilirubin), is not the same as that present in bile (cholebilirubin). Haemobilirubin remains combined with serum albumin and cholebilirubin remains in combination with glucuronic acid.

The main differences between the two bilirubins are summarised below:

Blood bilirubin (Haemobilirubin)	Bile bilirubin (Cholebilirubin)
1. Van den Bergh reaction is indirect or delayed direct.	1. Van den Bergh reaction is immediate direct.
2. Cannot be readily oxidised.	2. Easily oxidisable.

* **One unit of bilirubin** is equivalent to a concentration of 1 mgm of the pigment in 200,000 ml of serum.

Blood bilirubin (Haemobilirubin)	Bile bilirubin (Cholebilirubin)
3. Can be extracted with chloroform.	3. Cannot be extracted.
4. Warmth does not alter the quality of the Van den Bergh reaction.	4. Warming changes the reaction. Serum giving direct Van den Bergh reaction will give indirect reaction after short warming.
5. The molecules are larger and do not pass through a collodion membrane. [Because it remains combined with serum albumin.]	5. The molecules are smaller and can be easily dialysed through a collodion membrane. [Remains as Na bilirubinate.]
6. Renal threshold is much higher and is about 16–18 units (i.e., unless the concentration rises so high in the blood none will be found in the urine).	6. Renal threshold is only 4 units (4 units=1 mgm in 50,000 ml of serum).

Van den Bergh reaction. This test helps in detection of bile pigment in blood serum. There are three types of reaction:

(*a*) Direct. (*b*) Biphasic. (*c*) Indirect.

Two solutions are used in this test:

Solution I—Sulphanilic acid (0·1 gm), concentrated HCl (1·5 ml), distilled water—(100 ml).

Solution II—Sodium nitrate (0·5 gm) and water (100 ml) 25 ml of No. I solution is mixed with 0·75 ml of No. II solution—**Diazo reagent.** 1 ml of serum is taken in a small test-tube. To it equal amount of *Diazo reagent* is added and any one of the following reactions may occur:

1. **Direct reactions**

(*a*) Immediate or prompt—A bluish-violet colour immediately appears (within 10–30 sec.).

(*b*) Delayed—Reddish colour appears which gradually becomes violet and this takes from 5–15 minutes or even half an hour.

2. **Biphasic reaction.** A reddish colour appears promptly and after much longer time becomes violet.

3. **Indirect reaction.** At first 1 ml of serum is treated with 2 ml of 95% alcohol. It is shaken and centrifuged. 1 ml of supernatant fluid is taken and to it 0·25 ml of Diazo reagent is added. A reddish-violet colour appears immediately.

In *Jaundice* there is excessive accumulation of bile pigments in blood which causes yellowish discolouration of skin, mucous membrane and conjunctiva. There are *three* types of jaundice: (*a*) obstructive, (*b*) haemolytic, (*c*) toxic or infective jaundice.

In Obstructive Jaundice—Van den Bergh test is direct and prompt.

In Haemolytic Jaundice—Van den Bergh test is indirect.

In toxic or infective jaundice where there is parenchymatous liver damage—Van den Bergh test is delayed direct or biphasic.

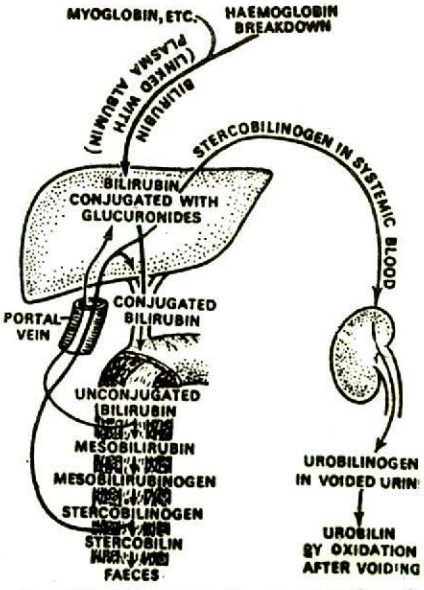


FIG. 316. Diagrammatic representation of pathways of bile pigment excretion (simplified)

After passing through the hepatic cells, conjugated *bilirubin* and *biliverdin* enter bile channels and then into the intestine along with bile. In the intestine following changes take place: *bilirubin→mesobilirubin→mesobilirubinogen→stercobilinogen.* On being exposed to air stercobilinogen is

further oxidised into yellowish-brown stercobilin and is responsible for the normal colour of the faeces. About half the amount of total bile pigments is excreted in the faeces, which varies from 40–280 mgm per day.

The remaining part of stercobilinogen is reabsorbed from the intestine and is carried back to liver. Under normal conditions, this reabsorbed stercobilinogen is almost fully re-excreted in the bile. A trace of stercobilinogen may fail to pass through the liver, and is excreted in the urine. This excretory product is named as urobilinogen which is quickly oxidised into urobilin by the air after the urine is voided (FIG. 316). It is believed that some urobilinogen passes directly to the kidney escaping the liver for excretion (not shown in FIG. 316). *Urobilinogen is identical with stercobilinogen and urobilin is identical with stercobilin.* Normally faecal excretion of bile pigments varies from 50–250 mgm per day, only 1–2 mgm being excreted through urine.

When liver is damaged, urobilinogen reabsorbed from the intestine, fails to pass through the liver cells and appears in the urine in a larger amount. Under such conditions, urine contains considerable amounts of urobilinogen and urobilin. *Presence of urobilinogen in urine in excess, therefore, indicates functional deficiency of liver.*

MECHANISM OF SECRETION OF VARIOUS DIGESTIVE JUICES

Introduction. There are five digestive juices, viz., *saliva, gastric juice, pancreatic juice, succus entericus* (intestinal juice) and *bile*, secreted from salivary, gastric, pancreatic, intestinal and hepatic gland respectively, which are poured in the alimentary canal at its different levels successively from oral to aboral side.

The term, **mechanism of secretion** is meant by (1) how the glands respond to secrete by the stimuli and how its flow and composition are maintained, (2) how the glands modify their secretion as regards their flow and composition by various types of stimuli and site of stimulation.

The **types of stimuli** are generally: (*a*) **nervous,** (*b*) **chemical:** (*i*) hormonal and (*ii*) other chemicals (diet, etc.), (*c*) **mechanical.**

Nervous stimuli are the stimuli, e.g., touch of food on the tongue or other parts of the G.I. tract, sight of food, smell of food, etc., act on the sensory nerve endings and thereby nervous impulses generated which pass *via* the central nervous system to trigger the corresponding motor nerve of the gland into action and the secretion takes place. Since the whole process is the unconscious so this type of secretion is reflex process.

Mechanical stimuli are those which stretch or distretch the organs, e.g., gas or food either solid or liquid and thereby stimulate the sensory nerve endings and local reflexes occur.

Chemical stimuli are the chemical substances which are due to (1) **intestinal hormones,** elaborated in the mucosa of pyloric part of the stomach or proximal portion of the small intestine, act on the gland passing through circulation, (2) **dietary food particles** partially digested act on the gland, (3) some intermediate metabolites may also act on the gland and secretion of glands takes place.

The existence of the chemical and its influence may be proved on the following way: (1) Isolation of the chemical substances in pure form, (2) In spite of the separation of the nerve supply of the gland whether

these chemicals can produce secretion, (3) Determination of the existence of mechanism for the release of chemical substances.

When viewed in this light, it will be seen that *mechanism of gastric secretion involves all these stimuli, excepting mechanical. Salivary secretion is purely a nervous process. Pancreatic secretion involves both nervous and chemical processes. Bile secretion is a chemical phenomenon with the possibility of a nervous one; while secretion of succus entericus (intestinal juice) involves all the three processes: nervous, chemical and mechanical.* The mechanical stimuli act through the local nerves.

The mechanism of each of the five secretions will now be described.

MECHANISM OF SALIVARY SECRETION

The **salivary centre** consists of superior and inferior salivary nuclei in the **reticular formation** of the medulla.

Nerve supply of salivary glands. The salivary glands receive double nerve supply—both from the sympathetic and the parasympathetic. The **parasympathetic fibres** *to the submaxillary (submandibular) and sublingual glands* arise from the superior salivary nucleus (dorsal nucleus of the VIIth cranial nerve) in the medulla as *nervus intermedius* and by-passing the

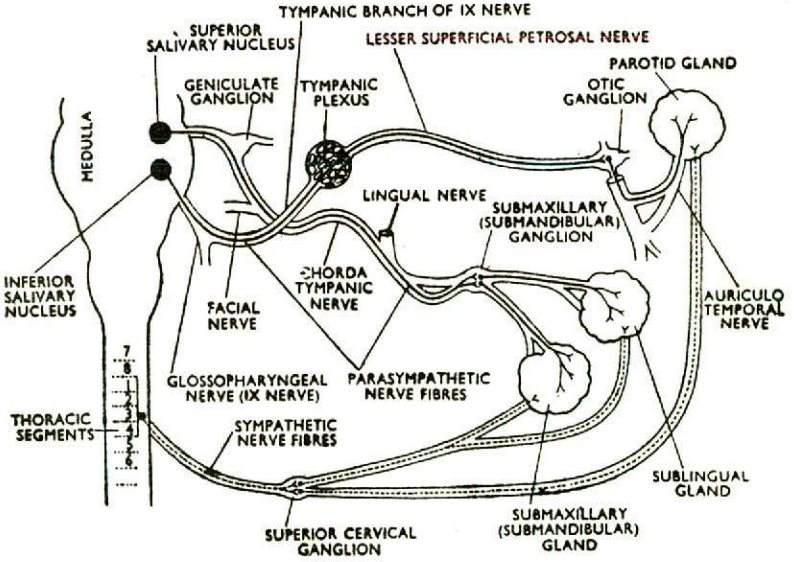


FIG. 317. Simplified diagrammatic representation of the parasympathetic and sympathetic innervations of the salivary glands.

geniculate ganglion descend downwards through the facial (VIIth cranial) nerve and then through the chorda tympanic branch of the facial nerve. The chorda tympanic nerve descends downwards and reaching the cavity of the mouth meets the lingual nerve. Then the secretory fibres leave the lingual nerve and end in the submaxillary (submandibular) ganglion (Langley's ganglion in animals). From the submaxillary ganglion the postganglionic fibres arise and reach the submaxillary and sublingual

glands and supply them with secretory and dilator fibres. The *parasympathetic* or *bulbar fibres to the parotid gland* arise from the inferior salivary nucleus (dorsal nucleus of the IXth nerve) in the medulla and descend downwards through the glossopharyngeal (IXth) nerve and being separated as the tympanic branch pass through the tympanic plexus and then through the lesser superficial petrosal nerve end ultimately in the otic ganglion. From this the postganglionic fibres arise and reach the parotid gland through the auriculotemporal branch of the fifth nerve to supply it with secretory and dilator fibres.

The **sympathetic fibres** to all these glands is derived from first and second thoracic segments of the spinal cord and come out through the first three or four anterior thoracic nerve roots and end in the superior cervical ganglion. The postganglionic fibres arise from this ganglion, pass along the walls of the arteries and supply all the salivary glands (FIG. 317). The sympathetic fibres are believed to end in the serous gland or in the serous part of the mixed gland and supply vasoconstrictor fibres to vessels of glands and myoepithelial cells of the duct.

Nervous control. On stimulation of the **parasympathetic nerves** in a cat the following effects are observed: (1) Secretion of water; (2) Vasodilatation. Parasympathetic nerve fibres act through the medium of acetylcholine and so they are known as **cholinergic fibres.** Hilton and Lewis have found that after stimulation of the parasympathetic fibres an enzyme (*kallikrein*) is liberated in the tissue fluid which acts on the proteins and form a polypeptide known as *bradykinin* which produces vasodilatation.

On stimulation of the **sympathetic nerves** the following effects are observed: (1) Secretion of viscous saliva with a higher solid content and (2) vasoconstriction. Sympathetic nerve fibres act through the medium of adrenaline and adrenaline-like substance and so they are known as **adrenergic fibres.**

Atropine blocks the action of acetylcholine, and has been used in medicine to inhibit salivary secretion. A diet rich in carbohydrate increases the salivary *amylase*. Of the endocrine secretions, adrenocorticotrophic hormone lowers the sodium concentration of saliva.

Significance of double nerve supply. Each glandular cell is supplied by two sets of nerves. Probably one helps in the secretion of fluid and salts, and the other for the secretion of organic constituents.

Some holds that the difference in action of these two sets of nerves are not due to their specific effect on the glandular cells, but are due to their different actions on the blood vessels. The sympathetic carries vasoconstrictor fibres; hence their stimulation will cause vasoconstriction in the gland and produce consequently less amount of saliva which becomes necessarily *thick*. Parasympathetic fibres will cause vasodilatation thus increasing the amount of saliva, which becomes necessarily *thin*.

Paralytic secretion. Claude Bernard observed that after section of the chorda tympanic nerve in a dog or cat, a scanty secretion of thin turbid saliva is produced which increases until the seventh or eighth day, at which it reaches a peak level, and diminishes about the third week. He called it as paralytic secretion. His presumption was that section of chorda tympani removed the restraining influence on secretion and as a result there was continuous secretion of saliva. Emmelin in 1952 explained that

paralytic secretion was due to increased sensitivity of the gland to adrenaline after section of the chorda tympanic nerve.

Experiments. For studying the mechanism of salivation, it is necessary to adopt certain experimental procedures, by which pure saliva unmixed with food, can be collected outside. This has been done in two ways: (1) A cannula is inserted into the parotid duct and through this all the saliva secreted by the gland is collected outside. (2) The opening of the duct is resected out and is shifted upon the outer surface of the cheek. Saliva can be collected outside through the opening (Fig. 318).

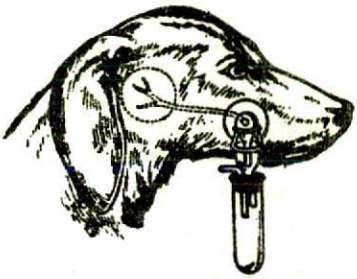


Fig. 318. Schematic representation of dog's parotid gland with fistula. For the collection of saliva is funnel along with a test-tube being fixed on the cheek at the opening of the glandular duct that brought out to the exterior.

With such preparations it is seen that when food is given to the dog salivation takes place, but when the corresponding nerves are cut salivation completely ceases. This proves that *salivation is a purely reflex phenomenon*. There is no direct chemical stimulus involved in it.

On further analysis, it is found that two types of reflexes are involved in salivation: (1) **conditioned** or **acquired reflex,** (2) **unconditioned** or **inherent** or **inborn reflex.**

It is believed that one type of reflex does not exclude the other, both are called into play together under ordinary condition.

Conditioned reflex. The existence of this reflex is proved by the fact that even the sight or smell of food can stimulate salivation, although no food is actually given. Various *conditioned* stimuli can be established which can produce salivation. Pavlov used to sound a gong just before giving food to the animal. After continuing this procedure for some days, it was seen that only the gong sound was sufficient to cause salivation even when no food was given. The gong sound here acts as the conditioned stimulus.

Unconditioned reflex. For this reflex, food should actually be given to the dog. The sensory stimulus for this reflex may arise from various sources as follows:

1. **From the mouth.** This is the chief place from which the normal unconditioned stimulus for salivation arises. The act of chewing, the sensation of taste, the irritation caused by the presence of food upon the mucous membrane of mouth—all these act as the sensory stimuli which reflexly produce salivation (Fig. 319). Here the effector is the salivary gland, the afferent path is represented in the trunks of the chorda tympani, the pharyngeal branches of the vagus and glossopharyngeal nerves, and the lingual, buccal and the palatine branches of the trigeminal nerve, the efferent path (*vide* p. 453) is the secretory fibres of chorda tympanic nerve with another peripheral relay station and its centre is the medulla.

2. **Oesophago-salivary reflex.** The sensory stimulus may arise from the oesophagus. When the food passes down the oesophagus, salivation is stimulated to some extent. Pathological conditions of oesophagus,

such as ulcer, cancer, or the presence of a foreign body in the oesophagus, stimulates salivation. If the distal end of cut oesophagus is stimulated, salivation occurs. If the vagi are divided, the reflex is abolished. The purpose of this reflex seems (*a*) to provide enough saliva necessary to wash away the irritating substance, and (*b*) swallowing of saliva will set up peristalsis-like movement of oesophagus which is likely to drive on the irritant. Oesophageal movement cannot be initiated by mechanical irritation but only when something is swallowed.

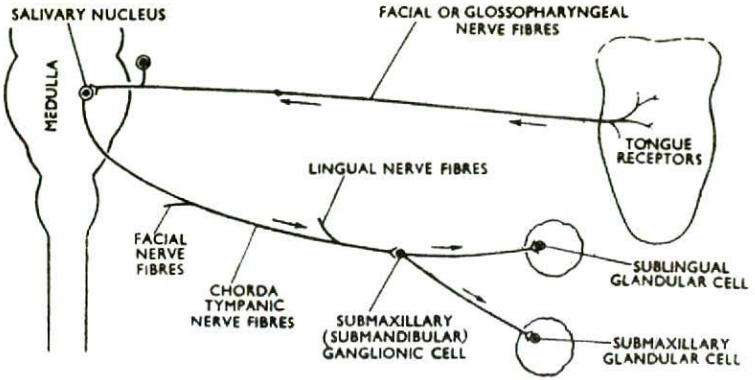


FIG. 319. Diagrammatic representation of the reflex pathways for the secretion of saliva.

3. **Gastro-salivary reflex.** The stimulus may arise from the stomach. Irritation of stomach stimulates salivation. When food is introduced in the stomach of a sleeping dog (to avoid psychic effects), salivation takes place after about 20 minutes. This is also seen in many irritating conditions of stomach, for instance, gastritis, gastric cancer, etc. Increased salivation, before vomiting, is a typical example.

4. **From other viscera.** It is possible that stimulus for salivation may arise in other viscera also. For instance, in pregnancy increased salivation occurs. It is believed that the sensory stimulus arises from the distended uterus.

Mechanical effects of mastication

As the food is chewed, the contractions of the muscles of mastication help to press out the saliva accumulated in the ducts and acini of the glands. Hence, mastication acts not as a real stimulus but through its mechanical effect.

To prove that salivation is a secretory process. Although in the saliva, there are certain products of excretion, such as the thiocyanates, urea, etc., yet, the following observations prove that salivation is mainly a secretory phenomenon:

1. **Saliva is extremely useful,** hence, cannot be an excretory product.

2. **Evidence of work.** During salivation the glands are found to be actively working. It is only to manufacture a secretion that a gland needs to undergo work. Excretory processes do not involve much work. The following facts prove that the glands are actively working: (*a*) During salivation

the *glands increase in size, become vascular* and their *temperature increases.* (*b*) The hydrostatic pressure in the salivary duct, during active secretion, may be double the amount of blood pressure in the carotid artery. Had it been a process of filtration, fluid ought to have passed from saliva into blood. But actually the reverse process takes place. *This shows that the glands are working against pressure.* (*c*) The osmotic pressure of blood is higher than that of saliva; so that fluid ought to have been drawn out of saliva and passed into the blood stream. But since salivation is just the reverse process, *the glands must be working against osmotic pressure.* (*d*) During salivation the amount of oxygen used and CO_2 produced by the glands, increase, i.e., the R.Q. value of resting gland is 0·6 to 0·8 increased to 1·0. This increase did not occur in the absence of glucose. Thus source of energy for salivary metabolism is glucose and to some extent fructose. This also is a very important evidence of work. (*e*) Saliva contains certain substances, which is not present in blood, viz., *ptyalin.* Obviously, *such things must have been manufactured in the glands.* This is a sure proof of secretory activity of the gland.

3. **Histological changes.** During activity a number of histological changes are seen in the gland. One important change is that, the *zymogen* and *mucinogen granules* which are present in the resting glandular cells, reduce to a much smaller number during activity. They take up water from the cytoplasm in the process of secretion and are released from the cells due to differences in osmotic pressure.

4. **Electrical changes.** Change of electric potential takes place in the gland during secretion. The outer surface of the gland becomes electrically positive to the hilus.

All these evidences prove that salivation cannot be a process of excretion; it is chiefly a secretory phenomenon.

Reflex control of rate of flow and composition of saliva. The receptor-centre-efferent system has got discriminating power so it can govern the salivary secretion, i.e., rate of flow and composition depend on the nature and intensity of the stimulus (e.g., food).

Spontaneous secretion. The continuous secretion of saliva without any known stimulus is termed as spontaneous secretion. Although its mechanism is not known but the acetylcholine may be the factor which is constantly secreted by the parasympathetic postganglionic nerve endings in small amount. Since atropine cannot check and cyanide or other metabolic poisons stop this type of secretion, so it is indicated that this is related and dependent to metabolic functions.

Adaptability of salivary reflex. The saliva secreted from the gland varies in both quantity and quality with the physical and chemical nature of the substances stimulating the secretion. The salivary gland does not secrete as a unit but different sets of epithelial cells of the gland contribute different components of secretion and their local productivity depends upon the intensity of excitation coming from the salivary centre. The afferent nerves are also different groups which carry impulse of specific nature and stimulate the different components of salivary centre which is a compound structure consisting of several parts and these in turn excite reflexly and selectively the different epithelial groups for appropriate types of secretion.

Disturbances of salivary secretion. The salivary secretion may be under certain conditions: (1) when decrease or absent called **hyposalivation,** (2) when increase called **hypersalivation.**

Hyposalivation: (*a*) Temporary—emotional state, e.g., anxiety, fear, fever and obstruction of the duct due to **calculi (sialolithiasis).** (*b*) Permanent—aptyalism is rare but when occurs is due to congenital hypoplasia or absence of the gland.

Hypersalivation—also called **sialorrhoea** occurs during (*a*) pregnancy; (*b*) neoplasm of the mouth, tongue, carious tooth, oesophagus, stomach and pancreas; (*c*) ulceration of oesophagus and stomach, spasm of stomach; (*d*) in neurological disorder, e.g., Parkinsonian disease and schizophrenia.

MECHANISM OF GASTRIC SECRETION

Gastric juice is a mixture of secretions of the different types of glands found in the stomach. As a whole gastric juice is acid in reaction, but when collected separately, it is found that, the *body and fundus secrete an acid juice, while the pyloric part secretes an alkaline juice.*

During fasting stomach secretes at a variable rate of 10–60 ml per hour. This juice is rich in mucus, poor in acid and contains pepsin. It probably acts as a mild antiseptic against swallowed bacteria. After meal gastric secretion is stimulated. On the average 500 ml of gastric juice is secreted per meal. The secretion starts almost immediately after food, reaches its maximum between one and a half to two hours, then gradually declines and comes to the fasting level after three to four hours.

Experiments. The mechanism of gastric secretion has been chiefly studied on animals. Some direct evidence has been obtained in man, from cases of accidental gastric fistula through which gastric juice could be collected. In man another method is often applied known as *fractional test meal.* This method is commonly adopted for investigating gastric functions in man at bedside.

In animals two very important experiments have been done for investigating the mechanism of gastric secretion: (1) the experiment of **sham feeding,** (2) the preparation of **Pavlov's pouch.**

Sham feeding (FIG. 320). The oesophagus of a dog is exposed and

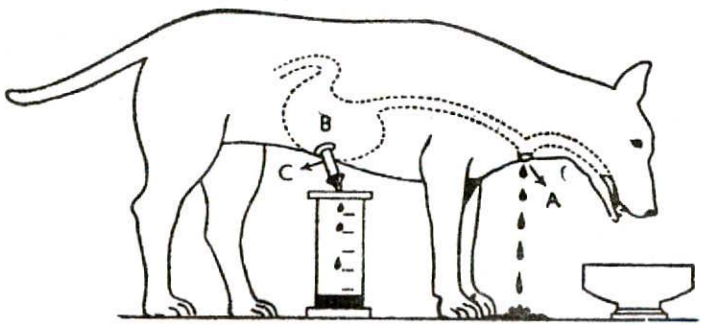


FIG. 320. SHAM FEEDING

A = opening of the divided oesophagus through which swallowed food is dropping out. B = body of the stomach with fistula through which gastric juice is coming out. C = cannula in the fistula.

divided in the middle of the neck and the two cut ends are brought to the surface. When the dog swallows food, the latter comes out through the upper cut end and does not enter the stomach. This experiment is very important to prove whether the food can stimulate gastric secretion even before entering stomach.

Pavlov's pouch (Figs. 321 & 322). It is a small diverticulum prepared from the body of the stomach and representing about one-eighth of the whole stomach. The pouch is prepared in such a way that its inner end is shut off from the main cavity of the stomach by two layers of mucous

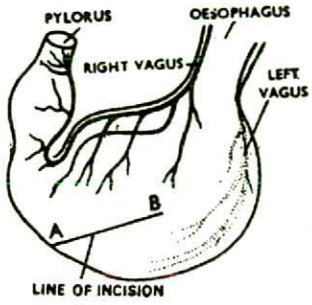


Fig. 321. Preparation of Pavlov's pouch for the study of gastric secretion where an incision is made that leaves the innervation intact.

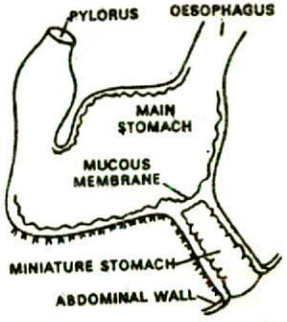


Fig. 322. Final stage after healing showing abdominal wall through which Pavlov's pouch is opening outside.

membrane while the outer end opens outside through an wound in the abdominal wall. During the surgical procedure least injury is done to the vessels and nerves, so that the pouch secretes a juice identical with that secreted by the body of the stomach. This preparation has got the following advantages: (1) Pure gastric juice can be collected from this pouch unmixed with food. This is a great help in studying the variations of gastric secretion—both in quality and quantity—as may be produced by different stimuli. (2) It is found in dogs, that the juice secreted by the pouch is always a constant fraction of the total amount of juice secreted by the main stomach. From this the total secretion can be found out.

Mechanism of secretion. From such studies it is found that gastric secretion can be divided into different phases: (1) the **nervous phase** (*cephalic phase* due to the arrival of impulse in the brain, i.e., head = cephalic), (2) the **gastric phase,** (3) the **intestinal phase.** The gastric and intestinal phases may be collectively called the **chemical phase,** because in these two phases the working stimuli are chemical substances, (4) Another one is an **interdigestive phase** and has also been studied. Each of these phases is briefly described below:

1. **Nervous phase.** A pouch of Pavlov is prepared in a dog and upon the same animal oesophagus is divided, as done in the experiment of sham feeding. The food, swallowed by the animal, comes out through the cut end of the oesophagus and does not enter stomach. In spite of it, it is found that the stomach secretes after a latent period of about 5–10 minutes and continues for as long as 1½ hours. When the vagi are cut this secretion fails to occur.

Stimulation of the vagus produces a secretion rich in pepsin and HCl, also some mucus, the most powerful action is possibly on acid secretion. The gastric cells are stimulated by acetylcholine released after vagal action. There is also a possibility that increased amount of **histamine,** liberated at the mucosa of stomach after vagal stimulation, stimulates the parietal cells. Vagal stimulation also causes vasodilatation of the gastric mucosa. Under certain conditions vagal stimulation can also stop or diminish gastric secretions. Stimulation of the vagus also increases the release of gastrin and augments the response of the cells of stomach to other type of stimuli.

Stimulation of the sympathetic nerves, supplying the stomach, causes *vasoconstriction,* but its effects on gastric secretion are not constant.

Hypothalamus exerts undoubted influence upon gastric secretion. Stimulation of hypothalamus increases gastric secretion by augmenting vagal activity. Hypoglycaemia has similar effect mediated in an identical way. Experimental lesions of hypothalamus have been found to produce gastric haemorrhages, erosions and even perforations. It is believed that some such lesion may be associated with the causation of gastric ulcer.

These show that the initial phase of gastric secretion is a reflex process and this type of secretion is called **appetite juice** by Pavlov. On further analysis it is seen that two types of reflexes are involved in it—(1) **unconditioned reflex,** (2) **conditioned reflex.**

Unconditioned reflex. The sensory stimulus for the unconditioned reflex arises in the mouth during chewing and swallowing of the food. The sensory nerves are the fifth, seventh and ninth cranial nerves. The motor nerve is the vagus. **Conditioned reflex (Psychic reflex).** The existence of conditioned reflex is proved by the fact that sight or smell of the accustomed food stimulates gastric secretion. Various other conditioned stimuli can be established which can arouse gastric secretion even when no food is actually given to the dog, i.e., without the contact of food in the mouth. The sensory nerves are those of special senses, viz., vision, smell and hearing. Motor nerve is the vagus.

The **appetite juice** has got the following characters: (1) It is rich in pepsin, acid in reaction and contains mucus. (2) *The composition of appetite juice is constant and does not vary with the type of food.* (3) The quantity varies with the intensity of appetite. (4) The secretion of psychic juice may be inhibited by shock, fear, anxiety, etc. (5) In animals it forms a considerable part of the total gastric secretion but in man the quantity is probably much less and is not essential. (6) Its importance lies in the fact that it helps to initiate the second phase of gastric secretion.

2. **Gastric phase** (*Hormonal*). At the end of sham feeding, gastric secretion elicited by *cephalic phase* dies away. But if food enters the stomach, further secretion of gastric juice takes place. The gastric phase of secretion is mediated by local and vagal reflex response to distention and also by the hormone gastrin released by the mucosa of the pyloric area. Thus when the stomach is completely denervated, this secretion is not affected. This proves that this secretion in addition to a nervous reflex and mechanical irritation of food on the gastric mucosa is due to a chemical stimulus. By further experiments it has been proved that a chemical excitant is actually operating in this phase and is called **gastrin** (FIG. 323). The following experimental facts can be put forth to uphold the gastrin theory. (1) Acid extract of pyloric mucosa, on injection, stimulates gastric secretion. (2) At the

height of gastric secretion, a substance is found to be present in the venous blood of stomach which can excite gastric secretion. (3) Ivy and Farrell cut out a small pouch from the body of the stomach and grafted it in the mammary region of a pig. The mammary gland being highly vascular, the graft easily sets there. The wound in the stomach is adequately sutured. With such a preparation it is seen that, when the second phase of gastric secretion is taking place in the main stomach, the grafted pouch also secretes gastric juice. Since there is no nervous connection between the stomach and the grafted pouch and there is no separate nervous connection (vagus motor) of the pouch, secretion in the latter must be due to a chemical excitant which is carried to the pouch through blood stream.

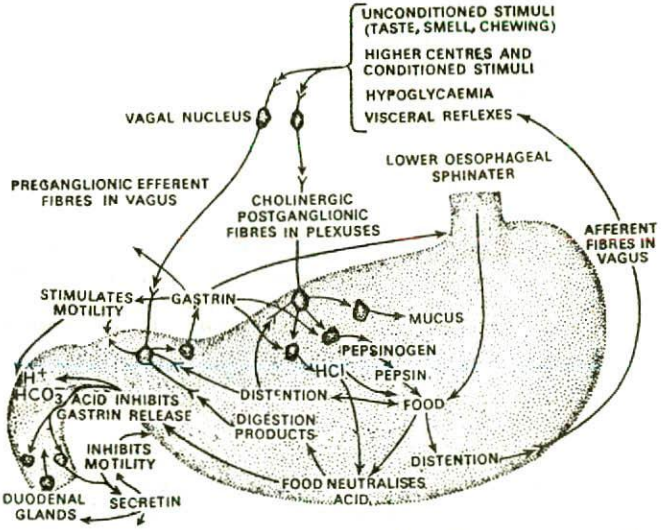


FIG. 323. Schematic representation of action of hormones controlling gastric secretion.

From *Physiology of the Digestive Tract*, by Horace W. Davenport, Year Book Medical Publishers, Inc. Used by permission.

(4) Komarov has isolated a protein derivative from the pyloric mucosa possessing strong stimulating effect on gastric secretion. (5) After resection of the pyloric part of stomach this phase of gastric secretion is greatly reduced. (6) When coagulated egg albumin, raw meat, undigested starch or fat, is introduced into the stomach through the gastric fistula or through the oesophagotomy wound of a sleeping dog (to avoid secretion of psychic juice) no secretion takes place. This proves that these substances neither have any mechanical effect nor carry the necessary chemical stimulus. But when meat extracts, liver extracts and partly digested meat, egg-white, etc., be introduced in the stomach, gastric secretion is stimulated. It has been demonstrated that stimulation of the vagus causes release of gastrin. This gastro-intestinal hormone is also liberated through a local reflex mechanism mediated through cholinergic nerves other than the vagus.

From these observations it can be concluded that gastrin is manufactured by the

pyloric mucosa from some products of protein digestion. This substance enters the blood stream, brought back to the gastric glands and stimulates their secretion.

Nature and action of gastrin. It is *polypeptide* in nature, two gastrins, **gastrin I and II,** differing in amino acid sequence have been isolated. Both of them stimulate gastric secretion. On injection, (1) gastrin stimulates gastric secretion—which is rich in acid but poor in pepsin, (2) it stimulates bile secretion, (3) it also stimulates pancreatic secretion to a slight extent.

The gastric phase of secretion constitutes the main part of gastric juice and continues for about three hours. *Unlike psychic juice, this part of secretion varies in quality and quantity according to the type of foodstuff.* The variations are as follows:

Response to food. (1) Meat increases both the quantity and the HCl content. (2) Bread stimulates a secretion having the greatest digestive power. (3) Fat inhibits secretion both in quality and quantity. [It also inhibits the movements of stomach.] This depressing effect may be due to a chemical substance called *enterogastrone.* [*Vide* below.] The inhibitory effects of fats are more strongly exerted from the duodenum than from the stomach. (4) Water, tea, coffee, spices, condiments, vegetable juices, etc., stimulate gastric secretion. (5) Mechanical distention of stomach by gas, such as with aerated waters, stimulates gastric secretion (and movements).

3. **Intestinal phase.** It was observed that the presence of certain food substance in the small intestine excites gastric secretion. The latent period is 2–3 hours but continues for 8–10 hours. When water, meat extract, peptone and partly digested proteins, etc., enter the duodenum in the process of digestion or are directly introduced into the duodenum (through a duodenal fistula), this secretion occurs. When these parts are completely denervated this phase of gastric secretion is not affected. This proves that it is due to a chemical stimulant, a hormone or secretagogue absorbed with the food from the intestine, the exact nature of the stimulus is not known.

Gastric secretion can also be *inhibited* by the presence of certain substances in the duodenum. For instance, (1) introduction of alkali directly into duodenum inhibits gastric secretion, (2) presence of fats in the duodenum inhibits gastric secretion (both the gastric and intestinal phases) This inhibitory action of fat is due to the liberation of an intestinal hormone called **enterogastrone.** *It inhibits gastric secretion and gastric motility.* Such an inhibitory agent has been detected in the blood of fat-fed animals and has been extracted from the intestinal muoosa.

Urogastrone is another inhibitory substance similar to, but not identical with enterogastrone. It has been isolated both from the urine of a normal male and from that of a pregnant womeh. *It exerts a specific inhibitory effect on gastric secretion* (for this reason its therapeutic use in the treatment of gastric ulcer has been recommended). Its role in the normal process of gastric secretion is not known.*

4. **Interdigestive phase.** Hydrochloric acid secretion has been found to take place at regular intervals, even in fasted man and dog.

* Certain other factors influence gastric secretion, such as (1) **Blood sugar**—low blood sugar stimulates and high blood sugar depresses gastric secretion. (2) **Insulin** stimulates gastric secretion by reducing blood sugar. (3) **Amino acids**—certain amino acids glycine, alanine, glutamic acid, etc., when given intravenously, increases gastric secretion. They all act by stimulating the nucleus of the vagus.

It has been observed that both hormonal and nervous mechanisms are involved in such secretion, the latter being mediated through the vagus. Recently, it is believed that the interdigestive phase is a part of intestinal phase and partly due to spontaneous secretion of saliva.

Hormones on gastric secretion. Hormones secreted by different endocrine glands influence gastric secretion. Glucocorticoids secreted by adrenal cortex stimulated by ACTH increases acid and pepsin secretion by the stomach but decrease the mucous secretion, and thus makes it more susceptable to ulceration. Epinephrine and norepinephrine, on the other hand, decrease gastric secretion.

Hypophysectomy causes characteristic changes in the chief cells of the gastric glands, consisting of a decrease in the size of nucleus and loss of most of the pepsinogen granules. Secretion of hydrochloric acid is also reduced.

Serotonin, possibly a hormone secreted by certain enterochromaffin cells in the intestinal mucosa, inhibits gastric secretion, particularly that activated reflexly or by cholinergic drugs.

Reserpine, which is used as a tranquiliser and in the treatment of high blood pressure, produces increased acid production in the stomach when given in a high dose for a long time. The mode of action is not clear.

Insulin acts through its effect on glucose metabolism and has an effect on the gastric glands similar to that of stimulation of the vagi. Release of gastrin is reduced by insulin.

Effects of various chemicals and drugs on gastric secretion. Numerous chemical agents and various drugs affect gastric secretion. Histamine is a powerful stimulant of gastric secretion. It is thought that it acts directly on the parietal cells. **Histalog,** an anlog of histamine, is also a powerful gastric stimulant.

Caffeine and **alcohol** are strong secretory stimulants, producing a juice of high acidity and rich in mucin.

Parasympathetic agents, such as acetylcholine, mecholyl, etc., are secretory stimulants.

Secretory depressants are also known. Alkali and acids depress gastric secretion, Belladona, atropine, hyoscine, etc., are secretory depressants.

Interrelation between the different phases. The phases of gastric secretion are closely interrelated. The appetite juice initiates gastric digestion, having a powerful digestive action on protein. *Secondly* due to the presence of food in the stomach gastrin is liberated which stimulates the gastric phase of secretion. Intestinal phase starts when stomach empties into duodenum. It probably ensures maximum gastric digestion of food. The value of enterogastrone lies in the fact that it stops rapid emptying of stomach and thus keeps fatty food for a longer time in the duodenal region, so that it may be properly mixed up with bile and pancreatic juice. A very small amount of gastric juice is secreted during the interdigestive phase.

Investigation of gastric secretion in man

The method which is commonly adopted for investigating gastric secretion in man is called **fractional test meal** or **gastric analysis.** The procedure is as follows:

The subject is given diet on the previous evening. In the next morning the patient is made to swallow a thin flexible rubber tube known as

the *stomach tube* (Ryle's tube, Lyon's tube or some other modification, (Fig. 324). The tube has got three markings on it. When swallowed up to the *first* mark coinciding with incisor teeth (about 30 cm or 12 inches from the end) the end is near the cardiac end of the oesophagus; if up to the *second* mark the end is within the stomach; when up to the *third* mark the end has entered the duodenum. During gastric analysis, the subject swallows the tube up to the second mark. The **resting contents** of the stomach are aspirated out and is preserved. Then the patient takes about a pint of oat meal gruel, the stomach tube remaining swallowed as it was. Every fifteen minutes a sample of about 20 ml is drawn out and the procedure is continued for three hours. Altogether thirteen samples are obtained, the resting contents being the first sample. Each sample is then tested for the following:

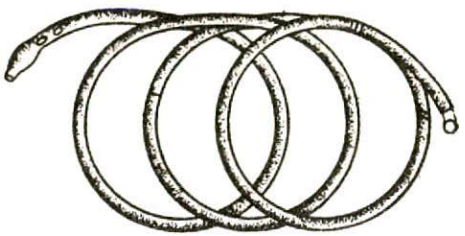


Fig. 324

1. **Free HCl.** Normally the free HCl of the resting contents lies between 1·5 and 2·0 mEq or 54–60 mgm (34·46 mgm=1 mEq) of HCl. After the gruel is taken the acidity is reduced by dilution. The free HCl then steadily rises and becomes maximum 40–50 mEq of HCl in the second hour. Then it gradually declines. When bile enters due to regurgitation, gastric acidity is reduced (Fig. 325). In gastric ulcer the value increases up to 3 times.

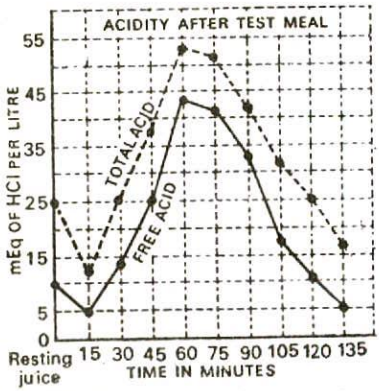


Fig. 325. Fractional gastric analysis in a normal subject showing normal curve (*after Best & Taylor*).

2. **Combined acidity.** This includes HCl combined with protein, mucus, etc., as well as organic acids such as lactic acid, produced by fermentation. Normally it varies from 10–55 mEq of HCl. In **hypochlorhydria** or **achlorhydria** the rate of fermentation is more, so that, this figure becomes high.

3. **Total acidity.** This is the sum total of free HCl, organic acids, combined acid and acid salts.

4. **Total chloride.** This includes free HCl, combined HCl and inorganic chlorides. Its importance lies in the fact that the free acid level is always disturbed by the entry of bile, but the total chlorides remain unaffected. Hence, estimation of total chlorides, along with estimation of free acidity, will give a more correct information about the secreting capacity of stomach.

5. **Starch and sugar.** Sugar is produced by salivary digestion of starch. Presence of sugar and starch indicates that stomach has not yet completely emptied. Their absence, therefore, indicates the emptying time. Normally, they are not found from the tenth or eleventh sample.

6. **Bile.** Presence of bile as indicated by yellow or green colour of the stomach contents, shows duodenal regurgitation. It also indicates that pyloric sphincter has opened and gastric emptying has begun. Generally bile first appears in the second hour.

7. **Blood.** It is not a normal constituent. Its presence shows ulcer, cancer or other haemorrhagic conditions of stomach. In case of ulcer the blood might be bright red or brown in colour and in case of cancer it is brownish-black.

8. **Lactic acid.** Derived mainly from fermentation of carbohydrate when there is a fall in the gastric hydrochloric acid. Hence, if free HCl is low, lactic acid will be high.

9. **Mucus.** Excess of mucus indicates an irritated condition of the stomach. [Gastritis, etc.]

10. **Presence of pepsin.** It indicates the functional condition of the peptic cells.

In addition to this, microscopic examination of each sample is carried out for *blood cells*, *epithelial cells*, *tumour cells*, *bacteria*, etc. Taking these facts into account a normal **gastric analysis curve** will be as shown in Fig. 326.

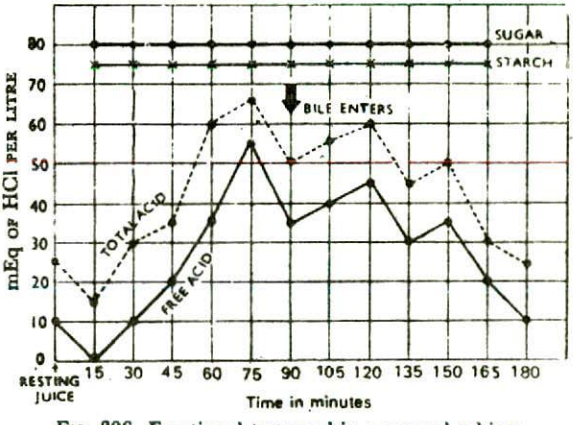


Fig. 326. Fractional test meal in a normal subject. Showing free HCl (maxm. 55 ml), total acidity (maxm. 65 ml), entry of bile (7th sample—1½ hours), presence of starch and sugar. Absence of starch and sugar in the 12th sample shows that the emptying time of stomach is 2 hours 45 minutes.

It will be seen from there that, this test not only gives an idea of the secreting capacity of stomach but the degree of motility (to be obtained from the emptying time), opening time of pylorus, duodenal regurgitation, etc., can be also known from it. In certain pathological conditions, characteristic variation of the curve is seen, viz., in gastric cancer and pernicious anaemia there will be achlorhydria, in duodenal ulcer the curve will be high 'climbing' type and so on.

To make a complete investigation of gastric functions only fractional test meal is not enough; radiological examination after *barium meal* has also to be performed. This will show the size, shape, motility, emptying time, presence of ulcer, etc., in the stomach. Other functional tests of stomach are as follows:

(*a*) **Histamine test of gastric secretion.** Histamine is a strong stimulant for the oxyntic cells. Only 0·5 mgm histamine chloride, injected subcutaneously, will stimulate gastric secretion at the rate of 200 ml per hour. In those patients who show achlorhydria with ordinary gastric analysis, this histamine test is performed in order to see the condition of the oxyntic cells. If performed in a normal subject, it shows the maximum

secretory capacity of the oxyntic cells. *Negative response* indicates atrophy of oxyntic cells.

(*b*) **Insulin test of gastric secretion.** Insulin reduces blood sugar which in its turn, stimulates vagus and thereby excites gastric secretion. A *positive insulin test* is proof of the presence of intact vagal fibres but a *negative result* is less conclusive since some subjects with intact vagi fail to secrete in response to insulin. However, the test is effective in most cases. Seven units of insulin given subcutaneously produce marked secretion of gastric juice (which is rich in HCl and pepsin content) although reduction of blood glucose by insulin to moderate degree causes inhibition of secretion. The secretion takes place after a latent period of 40 minutes. This test also shows the secretory capacity of stomach. Since the response does not occur in absence of vagus so the absence of gastric secretion following insulin induced hypoglycaemia is a test for the vagal denervation. A combined **insulin-histamine test** (7 units of insulin, followed 20 minutes later by 0·5 mgm of histamine) is also advocated by some, to test the maximum secretory power of the gastric mucosa.

In about 2–5% of normal healthy people neither any HCl nor any pepsin is found in the gastric juice. This condition is called **achylia gastrica.** This is a congenital error due to non-development of oxyntic and peptic cells. This condition does not affect health. Because, pancreatic enzymes can digest all the ingested foodstuffs. In certain pathological conditions (pernicious anaemia, cancer of the stomach, etc.), the acidity is very low (**hypochlorhydria**) or it may be altogether absent (**achlorhydria**). On the other hand, some people may have higher acidity in the gastric juice (**hyperchlorhydria**). In females the acidity is proportionally lower than in males. In the infants and children it is much lower than in adults. In men after thirty and women after fifty both free and total acidity gradually decline. A high gastric acidity is generally associated with hypermotile stomach. In people with poor muscular built and sedentary habits the acidity is low.

ORIGIN AND CHARACTER OF THE IMPORTANT CONSTITUENTS OF GASTRIC JUICE

1. **Hydrochloric acid.** This is secreted by the **oxyntic cells** (parietal cells). They are present in the fundus and the body of the stomach. There are many theories regarding formation of HCl. The views of Davenport, Davies and others explain the formation of HCl in a simplified way. According to them, the H^+ and OH^- ions are formed by ionisation from water or other metabolites. H^+ ions are passed out of the oxyntic cells into the canaliculus of gastric gland. This is an active process, the energy for which is derived from aerobic and anaerobic glycolysis. The secretion of HCl stops when energy conversion is blocked by DNP, etc. The transport is also dependent on oxidative phosphorylation. For each H^+ ion released, one OH^- ion is held back in the cell. This OH^- ion combines with the H^+ ion released from dissociation of H_2CO_3 into HCO_3^- and H^+, the HCO_3^- being released in the circulation. The H_2CO_3 is formed in the cell by the combination of CO_2 and H_2O, the reaction being catalised by the enzyme **carbonic anhydrase,** present in the gastric cells in large amounts. Since blocking the action of carbonic anhydrase by diamox, the HCl formation stops, so carbonic anhydrase plays an important role in the HCl formation. After meal there is an increase in pH of systemic blood and urine due to liberated HCO_3^- and is named as **alkaline tide.**

The secretory mechanism is an active process and consists of at least four parts:

1. Aerobic and anaerobic reactions produce high-energy phosphate bond ($\sim$P) which provides energy for driving the secretory reaction. Compounds such as fluoro-

acetate which stops TCA cycle and interferes energy formation and DNP which makes ~P unavailable for work (without reducing O_2 consumption) inhibits acid secretion.

2. The secretory reactions proceed in three stages: (*a*) One ~P combines with reduced low-energy precursor to produce a reduced high-energy precursor, (*b*) This high-energy compound is oxidised yielding H^+, an electron and a low-energy precursor. The

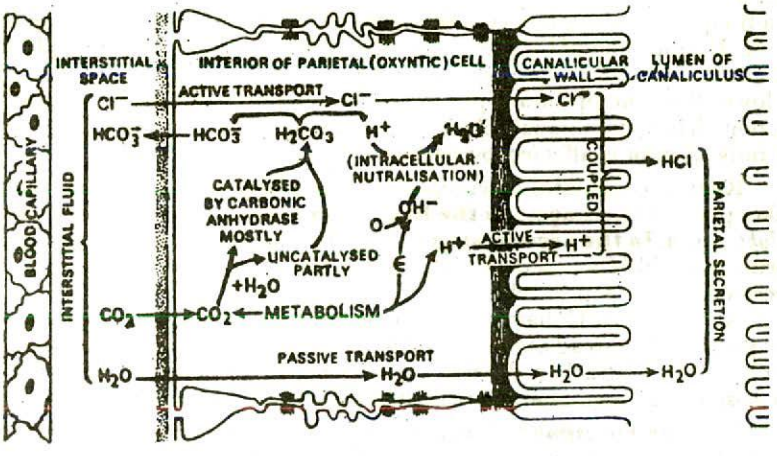


FIG. 327. Diagrammatic representation of the mechanism of secretion of hydrochloric acid by parietal cell.

energy is utilised in transporting the H^+ against concentration gradient (0·00005 mN in plasma to 150–170 mN in gastric juice). (*c*) The oxidised low-energy precursor is reduced by substrate electrons and is available for reaction 2(*a*).

3. The electron liberated in reaction 2(*b*) is accepted by oxygen producing hydroxyl ions.

4. The OH^- produced are neutralised by acceptance of proton from buffers, produced as ($CO_2+H_2O \rightarrow H_2CO_3 \rightarrow H^+ + HCO_3^-$) in presence of carbonic anhydrase, which forms water ($H^+ + OH^- = H_2O$). The HCO_3^- passes to the blood and urine increasing the pH, which is known as **alkaline tide.**

2. **Pepsin.** (*a*) Manufactured by peptic cells. (*b*) In the resting cells it is present in the form of zymogen granules as **pepsinogen.** During secretion these granules disappear. (*c*) Pepsinogen has been isolated in pure form. (*d*) Pepsinogen is converted into active pepsin by any solution having an acidity stronger than pH 6·0. Under normal conditions, HCl of gastric juice activates pepsinogen into pepsin. But any other inorganic acid will also do it. (*e*) In the process of activation, about 15% of the nitrogen content of the pepsinogen molecule is lost. (*f*) Pepsin is inactive in neutral or alkaline medium, but it is highly *proteolytic* in strong acid solutions. On the average, the optimum pH lies between 1·5–2·0. (*g*) The optimum pH varies with the nature of protein to be acted upon. For instance, for albumin and globulin it is about 1·5; for casein 1·8, for gelatin 2·2 and so on. (*h*) Pepsin is protein in nature. (*i*) It acts upon proteins and converts them up to peptone, but not to free amino acids. (*j*) Pure crystalline pepsin can also act like rennin and coagulate milk. (*k*) An enzyme **gastricsin** having about one-fourth the activity of pepsin is secreted by gastric cells. Optimum pH of this enzyme is pH 3·0. (*l*) Another proteolytic enzyme **cathepsin**

(optimum pH 4·0) has also been found in the gastric juice. (*m*) Human blood and urine contain **uropepsinogen** derived from the stomach. The uropepsin of strongly acid urine has proteolytic property.

3. **Rennin.** Rennin is a separate enzyme present in the stomach of calf and other young animals at least, and has milk-coagulating action. It is a thioproteose (sulphur-containing proteose). It has been isolated in pure form. Its optimum pH is 6·0–6·5, so that the high gastric acidity (pH 2·0) in adults inactivates this enzyme. Infant's stomach also has a pH which is lower than the optimum pH for rennin activity, and most possibly this enzyme has no functional role in human beings. The clotting and digestion of milk in man is affected by pepsin.

Rennin coagulates caseinogen with the help of Ca ion. The action takes place in two stages: **In the first stage** rennin converts *caseinogen* into *soluble casein*. **In the second stage** Ca ion combines with soluble casein and forms insoluble Ca caseinate. This is the clot. It is believed that rennin is secreted by the peptic cells.

According to Hollander, it is suggested that there is single enzyme for proteolysis instead of many which may have two or more active centres, each of which attacks a different type of peptide linkage at different pH so possesses its own characteristic pH curve.

4. **Gastric lipase.** It is a weak fat-splitting enzyme, quite distinct from the lipases of pancreatic juice and succus entericus. Gastric lipase is a *tributyrase* and acts on butter-fat *tributyrin*. Lipase acts best in a slightly acid medium (optimum pH 4·0–5·0) and is destroyed by alkali or high acidity. Hence, this enzyme is not of much importance in adults where the gastric acidity is high. In infants, gastric acidity being low, tributyrase enzyme is important for digestion of their staple food—milk. This also is probably secreted by the peptic cells.

5. **Gastric mucin.** Mucin is secreted chiefly by the cells in the pyloric region and to some extent by the mucous cells and goblet cells in the body and fundus. Visible mucus is secreted by the surface epithelial cells of the gastric mucosa and is thick, viscous and even jelly-like. It forms a transparent coating over the surface of the gastric mucosa. Soluble or transparent mucus is secreted by the cells of the pyloric and cardiac glands, and also by the mucous neck cells of the fundic glands. It is a constituent of pure gastric juice (*dissolved mucin*). *Mucin is a* **glycoprotein.** It serves certain important functions: (*a*) It acts as a buffer and has a high acid-combining power. Thus it reduces high gastric acidity and prevents injury to the gastric mucosa. (*b*) To some extent it inhibits peptic activity and this action is due to the presence of mucoitin sulphuric acid in it. (*c*) By forming a coating on the mucous membrane it protects the latter from the injurious effects of the gastric juice. (*d*) It also acts as a lubricant.

A gastric-secreting inhibition has been isolated from the gastric juice of patients with achlorhydria and pernicious anaemia. The nature of this inhibition is not known, but it was found in the mucin fraction of gastric juice of normal man although the potency is greater in these patients. The exact nature is not known. This secretory inhibitor has also been isolated from human saliva and the name has been given as *gastrone*. Gastrone can inhibit secretion stimulated by histamine or gastrin. It may have some relation to the neuropoietic factor explained below.

6. **Intrinsic factor.** A heat-labile **mucoprotein** possibly secreted from neck chief cell is responsible for the proper absorption of vitamin B_{12} (extrinsic factor). Absence of this causes pernicious anaemia. Secretion of this factor takes place before HCl or pepsin.

7. **Neuropoietic factor.** As pernicious anaemia is often associated with subacute degeneration of spinal cord, it has been suggested that the stomach might produce a factor responsible for nutrition of the nervous system.

Pancreas

The pancreas is both an *endocrine* as well as *exocrine* gland. It is devoid of distinct connective tissue capsule and is covered by a fine layer of the loose tissue which passes into the gland as septa and subdivides the gland into many lobules. In lower animals (cat) the lobules are completely separated from one another by the connective tissue.

The *exocrine component portion of the pancreas* is a compound tubular gland. The terminal secretory portions of this gland are known as *acini* or *alveoli* which are tubular and somewhat convoluted and secrete pancreatic juice. These acini resemble those of serous (serozymogenic*) alveoli of salivary glands and do not contain myoepithelial cells. The main excretory duct of the gland is the *duct of Wirsung*, which extends the entire length of the gland, giving out several intralobular ducts or intercalated ducts. The duct of Wirsung opens in company with the common bile duct into the *ampulla of Vater*, which opens into the second part of the duodenum. An accessory pancreatic duct, *duct of Santorini*, is often present. Within the lumina of many acini, one or more cubical cells are lying in contact with the apices of the secreting cells. These cells are known as *centro-acinous (-acinar) cells*. The cytoplasm of this cell does not possess any secretory granules. In each secretory cell, there are two well-marked zones—an inner (apical) zone towards the lumen and the outer (basal) zone towards the basement membrane. In the inner zone there are numerous course *zymogen granules* and their number are varying with the functional activity of the cell. Their number are diminished during digestion but increased during rest. The basal zone contains the nucleus as well as basophilic or chromophilic substance. Electron microscopic structure shows highly developed rough-walled endoplasmic reticulum and a supranuclear Golgi apparatus. Surface membranes are studded with *ribosome granules* which give basophilic staining. In resting stages the granular zone gradually increases up to three-fourths of the cell, but during activity the granular zone gradually diminishes in size. The pancreatic excretory duct is also similar to that of the salivary gland. Larger ducts contain elastic fibres and plain muscles which, when contract, may prevent the flow of juice into the duodenum. Near the duodenum small mucous glands are seen in the lamina propria.

Zymogen granules contain pro-enzymes. The pro-enzymes become activated on secretion to form enzymes. These enzymes are responsible for latter stages of digestion of proteins, carbohydrates and fats.

Between acini or alveoli there are found groups of solid cells, termed as *interacinous (interalveolar) cell islets* (or **islets of Langerhans**) which is the *endocrine component portion of the pancreas*. The islets (islands) vary in size and are shown by drawing from the *exocrine tissue* by a thin basement membrane.

* It refers to the cells whose serous secretions are known to contain an enzyme.

The *endocrine* pancreatic tissue cells are formed with much less cytoplasm than those of the *exocrine* pancreatic tissue cells. These islets are scattered throughout the pancreas but more numerous in the tail than elsewhere. There are two main types of cells in the islets: α- and β-cells (FIG. 328). The β-cells contain numerous insulin granules and secrete **insulin.**

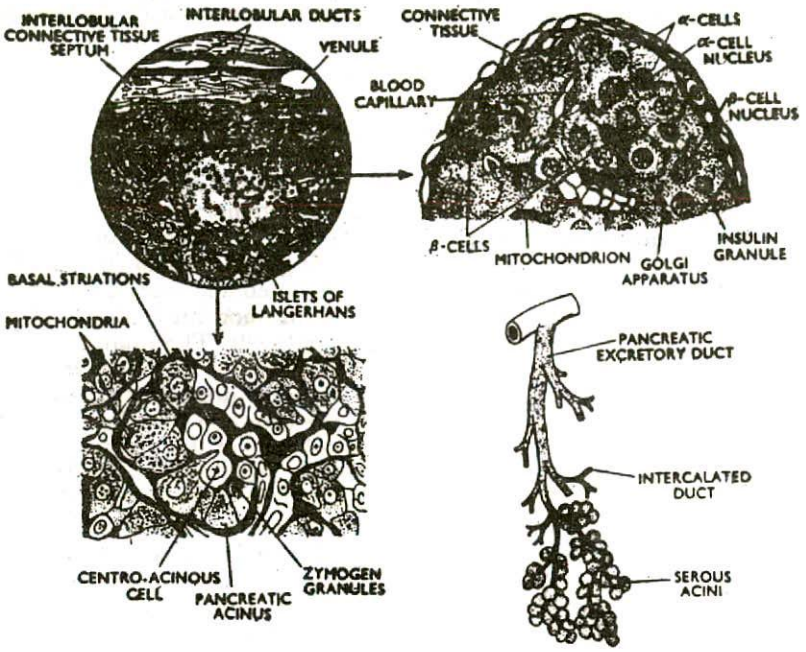


FIG. 328. Diagrammatic representation of the pancreas including its exocrine and endocrine components.

Recent studies by Steiner and his colleague Oyer showed the existence of a *biosynthetic precursor of insulin* termed **proinsulin.** The concept of proinsulin is supported by the following evidences:

1. Oxidative regeneration of reduced proinsulin is much more efficient than that of reduced insulin.
2. Pancreas slices incorporate labelled amino acids into proinsulin fraction first.
3. Low concentration of trypsin readily cleave sensitive bonds in proinsulin giving a insulin-like product.

The α-cells contain *glucagon granules* and secrete **glucagon.** A few γ- and δ-cells are scattered in the islets. According to Hellerström et al it reveals that α-cells can be classified as α_1 which is argyrophilic and α_2, non-argyrophilic but rich in protein-bound tryptophan.

Development. Pancreas develops as an outgrowth of the endoderm of the small intestine and ultimately becomes hollowed out to form the alvéoli or acini. The islets of Langerhans develop as buds from the ducts and remain as solid clumps of cells. During development in most cases, the connections with the duct vanishes and the islets become completely isolated. But in a few cases the connections persist as solid chords.

MECHANISM OF PANCREATIC SECRETION

Experiments. Most of our knowledge regarding pancreatic secretion has been derived from experiments on animals. Some direct evidence in man has been obtained from cases of accidental or postoperative duodenal fistula, through which pancreatic juice could be collected outside. In dog the process is studied by establishing a pancreatic fistula by cutting out the duodenal papilla (through which the duct opens) which is brought to the surface and sutured to an opening in the abdominal wall. The duodenal wound is stitched up. Pancreatic juice is collected by a cannula inserted into the duct. In man some information may be obtained with the help of a duodenal tube (Ryle's tube swallowed up to the third mark).

With these experiments it is seen that during fasting there may not be any secretion for long periods. Occasionally a little secretion takes place. The rate of secretion actually starts 1–2 minutes after taking food. The rate of secretion steadily rises, lasts for about three hours and then gradually declines. Greatest increase of secretion is observed at the time when gastric contents enter duodenum. This indicates that the acid chyme of the gastric juice exerts a stimulant effect on pancreatic secretion.

On closer study it is found that pancreatic secretion consists of two phases: (1) **nervous phase,** (2) **chemical phase.**

Nervous phase. Pancreatic secretion starts 1–2 minutes after taking food. When the vagi are cut, the secretion is abolished. *This proves that the initial phase of pancreatic secretion is a reflex response.* The *stimulus* for this reflex arises *in the mouth* during mastication as well as *in the stomach* when food enters the latter **(gastro-pancreatic reflex).** It is to be noted that this reflex is purely *unconditioned. There is no conditioned stimulus here.* This stands in great contrast with the nervous phase of gastric secretion. That the vagi are the

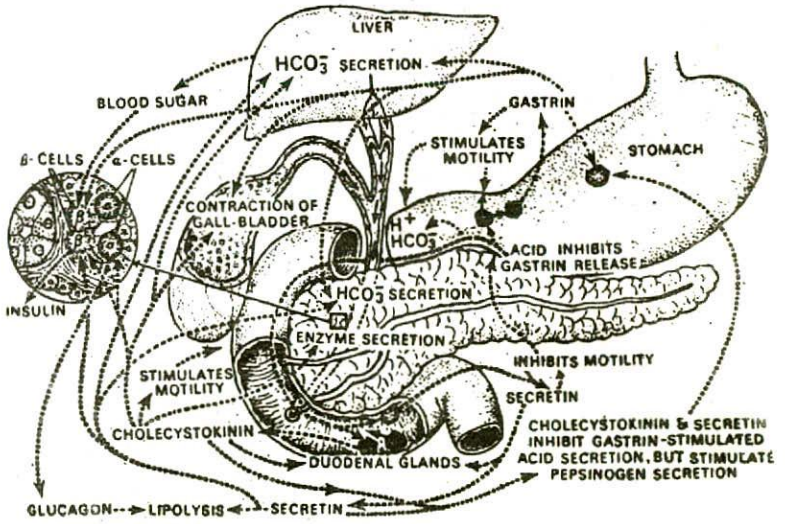


FIG. 329. Schematic representation of action of hormones controlling of pancreatic and hepatic secretions.
From *Physiology of the Digestive Tract,* by Horace W. Davenport, Year Book Medical Publishers, Inc. Used by permission.

motor nerves of pancreas is proved by the fact that when they are stimulated, increased pancreatic secretion takes place. This *vagal secretion is rich in enzyme* but has very little effect on bicarbonate concentration. In addition there is a local cholinergic reflex mechanism independent of vagal innervation. Thus, the vagal juice has got a greater digestive power. Acetylcholine is the mediator and parasympathomimetic drugs, e.g., pilocarpine are also effective. The response is blocked by atropine. Inhibition of secretion may also be obtained by stimulating adrenergic nerves producing vasoconstriction and constriction of ducts. Thus stimulation of sympathetic nerves may decrease secretion of pancreatic juice by reducing the blood flow through the organ and flow of juice through the duct.

Chemical phase. There are many controversial opinion regarding the cell responding to a stimulus with a characteristic type of functional activity regardless of the nature of stimulus. It is now thought that the cells of intralobular ducts secrete water and bicarbonate and the enzymes are secreted by acinous cells. It has already been noted that the rate of secretion of pancreatic juice rises sharply when the gastric contents enter duodenum. This is the onset of chemical phase. Bayliss and Starling isolated a loop of jejunum maintaining its vascular supply intact but destroying all possible nerve connections. When acid was introduced into this loop, pancreas was found to secrete. Since there is no nervous connection between this loop and the pancreas, it is evident that the stimulus must be carried to pancreas through blood stream. That HCl itself is not the stimulus is proved by the fact that injection of the acid into the portal vein did not produce any effect. But when acid extracts of intestinal mucosa were injected into the portal vein, pancreatic secretion was stimulated. This proves that the acid liberates some substance from the mucous membrane which acts as the real stimulus. This substance is called *secretin* originally by Bayliss and Starling. Recently this has been separated into the following different components: (*a*) **Secretin,** (*b*) **Pancreozymin,** (*c*) **Hepatocrinin** stimulates liver to secrete bile. (*d*) **Cholecystokinin** causes contraction of gall-bladder and (*e*) **Enterocrinin** stimulates release of intestinal juice. The first two which are related to the pancreas are described below.

Nature and action of secretin. It can be extracted from the mucous membrane of the duodenum and upper part of the small intestine with water, 0·4% HCl, soap solution or dilute alkali. From the nature of the solvents it is obvious that during normal process of digestion secretin can be extracted by the HCl of the gastric chyme as well as by the alkali of bile. Secretin has been isolated by

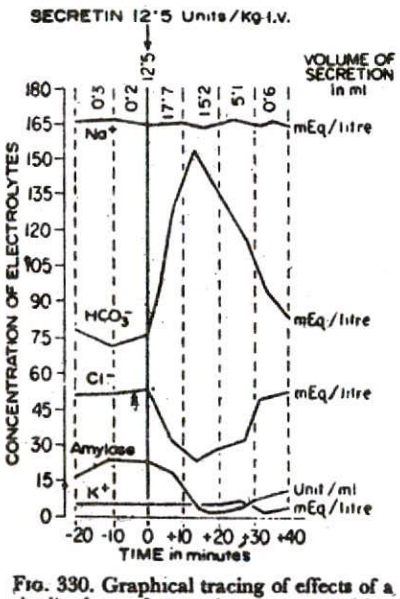


FIG. 330. Graphical tracing of effects of a single dose of secretin on composition and volume of the pancreatic juice (*after Ganong*).

various workers and is believed to be a *polypeptide*, containing 27 amino acid residues. Its molecular weight is about 5,000. It is rapidly destroyed by pepsin and trypsin in alkaline or neutral medium. It remains stable in acid solution. Recently secretin has been synthesised. When secretin is injected intravenously, the flow of pancreatic juice increases (FIG. 330). *This juice is watery, rich in bicarbonate but poor in enzyme.*

Pancreozymin. It is a polipeptide containing 33 amino acids. This causes release of zymogen granules from the pancreatic acinous cells resulting in release of a pancreatic juice rich in enzymes but poor in bicarbonate.

Influence of various foodstuffs on pancreatic secretion. It has been observed that pancreatic secretion remains high for about three hours and then declines. This is due to the fact that stomach is completely emptied within three hours when mixed meal is ingested so contact of gastric chyme is lost with the mucosa of proximal part of the small intestine.

Pancreatic juice is found to vary in quality and quantity with different types of food. Meat stimulates a *secretin type of response*, i.e., large volume, more alkali and less enzyme. Fat elicits a *vagal type of response*, i.e., moderate volume, low alkali and rich in enzyme. Bread produces a mixed type of response.

MECHANISM OF BILE SECRETION

Experiment. In man bile secretion has been studied in cases of accidental or postoperative biliary fistula. Most of our knowledge has been derived from observations on dogs. Pure bile can be collected in two ways—by (1) **preparing a permanent fistula in the common bile duct,** (2) **altercursive intubation** (McMaster and Elman). This experiment is of great advantage, because, all bile can be collected outside and when necessary, can again be allowed to pass into the small intestine. So that the normal process of digestion and absorption is not disturbed and thus the animal may live a normal life for many months. In the first experiment no bile could enter the small intestine and hence the animal dies in a short time due to nutritional disturbances.

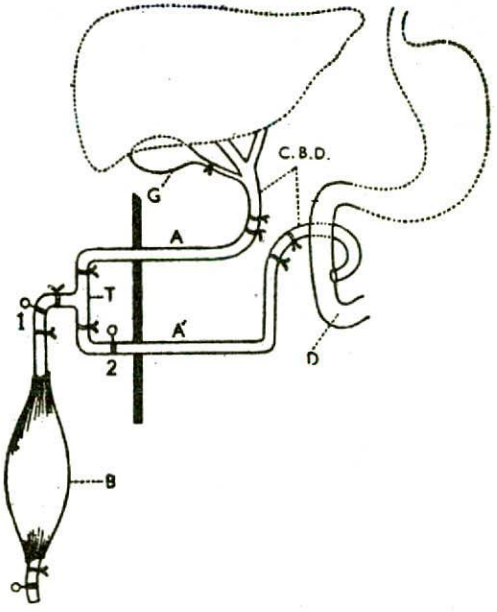


FIG. 331. ALTERCURSIVE INTUBATION.
G=gall-bladder with the cystic duct tied. C. B. D.= the two parts of the divided common bile duct. A & A'=tubes inserted in the upper and lower parts of the divided common bile duct respectively. T=three-way tube. 1, 2=adjustable clips. B=bag; D=duodenum. When clip 1 is open and 2 is closed, bile flows into the bag B. When 1 is closed and 2 is open, bile enters the duodenum.

In altercursive intubation (FIG. 331) the common bile duct is divided in the middle and the two ends of a long flexible rubber tube are inserted into the two cut ends of the common bile duct. The tube is held *in situ* by appropriate ligatures. The middle part of the rubber tube is brought outside through an opening in the abdominal wall and fitted to a three-way tap. Clips are placed in suitable places and by adjusting them, bile can either be collected outside or may be allowed to enter duodenum. The cystic duct is tied to prevent entry of any bile into the gall-bladder. With this preparation the normal course of bile secretion, its amount variations with different types of food, influence of nerves, influence of various other chemicals have been studied.

From such observations the following facts about bile secretion are known:

(1) The phenomenon of bile secretion by the liver is an active and continuous process, but its entry into the duodenum is intermittent, and takes place only during digestion. Contraction of the gall-bladder starts a self-sustaining mechanism for expulsion of bile and indirectly stimulate bile secretion. After digestion is complete, the sphincter of Oddi closes, breaking the cycle (FIG. 332).

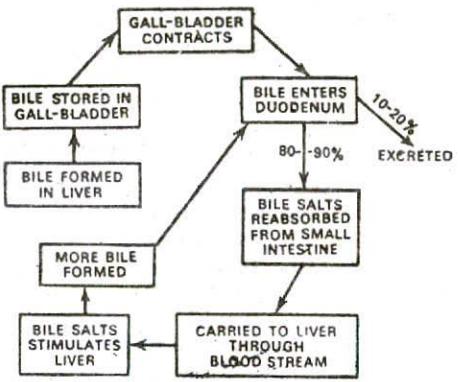


FIG. 332. Block diagram showing regulation of bile secretion.

(2) About 800–1,000 ml of bile is secreted by an average adult per day.

(3) The total amount bears a direct relation with the body weight,—the rate of secretion being 15 ml per Kg of body weight per day.

(4) The rate of secretion increases markedly about one hour after food, reaches its maximum between 2–5 hours and then declines. At the end of intestinal digestion and absorption it comes down to the normal resting rate.

Mechanism of secretion. *Bile secretion is practically independent of nervous influence. The normal stimulus for bile secretion is almost wholly chemical in nature.* Any agent which increases the flow of bile into the intestine is known as a **cholagogue.** A *choleretic* is an agent which increases the output of bile from the liver without necessarily changing its constitution, and a hydrocholeretic causes an increase in the volume of bile without corresponding increase in bile solids. The following substances are found to stimulate bile secretion.

(*a*) **Bile salts**—*These are the most powerful choleretic.* They act as the main stimulus in the normal process of bile secretion during digestion. Bile salts absorbed from the intestine are carried to the liver and re-excreted. This is known as *enterohepatic circulation.* The taurocholic acid is more powerful than glycocholic acid. When they are given by mouth or injected intravenously marked increase of bile secretion takes place. They increase the amount of bile as well as the total solids. (*b*) **Influence of foodstuff**—

Fats and proteins stimulate bile secretion, carbohydrates have no such effect. The exact process by which fats and proteins stimulate bile secretion is not known.

Secretin increases bile flow but doubtful. So it is suggested that hepatocrinin may be a specific liver hormone present in intestine released by the action of food.

It has been noted that bile secretion increases about one hour after meal, remains high for about 2–5 hours and then declines.

MECHANISM OF STORAGE OF BILE

Bile secretion by liver is an active and continuous process, but its expulsion in the duodenum is intermittent. These facts necessarily prove that after secretion bile must be stored somewhere. *The gall-bladder is the chief place for bile storage.* The common bile duct, which is shut off from duodenum by the *sphincter of Oddi*, may hold some bile. When the pressure of bile in the common bile duct rises to about 70 mm of water, bile begins to pass into gall-bladder. The gall-bladder has got a special capacity of absorbing water and slightly the inorganic salts (FIG. 333). Due to this property it can concentrate bile nearly ten times. The average capacity of gall-bladder is about 50 ml. Since bile is ten times concentrated, 50 ml of bladder bile is equivalent to 500 ml of duct bile. Thus gall-bladder acts as a very efficient reservoir. It can store large amount of bile without any appreciable rise of pressure.

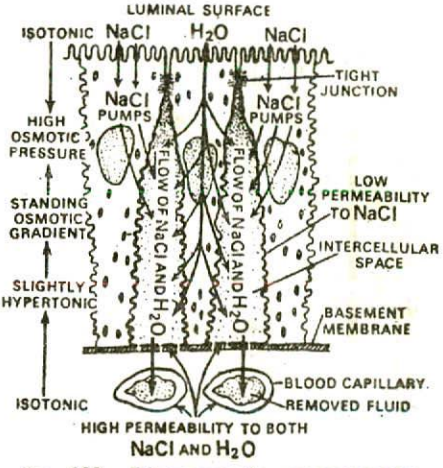


FIG. 333. Diagrammatic representation of mechanism of fluid transport by the gall-bladder (diagrammatic).

MOVEMENTS OF GALL-BLADDER

Experiments. In animals it can be studied by exposing the gall-bladder, draining all bile from it and filling it with iodised oil which is opaque to X-ray. Its movements are then studied with X-ray, under different conditions. In man it can be studied by administering an X-ray opaque substance—tetra-iodophenolphthalein, which is excreted through bile. The movements are then observed under X-ray.

Under fasting conditions gall-bladder shows weak and irregular contractions which are not strong enough to expel bile in the duodenum. After food, active contractions begin in about 5–30 minutes. The contraction continues intermittently till gall-bladder is empty. The normal emptying time varies from 2–5 hours.

MECHANISM OF EXPULSION OF BILE

Experiment. It is best studied in animals by the experiment of **triple intubation** as devised by McMaster and Elman (FIG. 334). In man it can

be studied by giving *tetra-iodophenolphthalein*, (which is excreted in bile and is opaque to X-ray) and then noting the alteration of size of gall-bladder under X-ray—**cholecystography.**

During fast there is no expulsion of bile, because the gall-bladder contractions are weak and the tone of the sphincter is high. When food is seen or taken, contraction of gall-bladder starts and at the same time, the resistance of the sphincter is reduced. The pressure in the bile duct rises to about 200 mm of H_2O and bile is momentarily expelled. This expulsion of bile is probably assisted by the contraction of the ampullary part of the common bile duct. Under normal conditions the sphincter can withstand a pressure of about 100–120 mm of H_2O. After 24 hours fasting or with a carbohydrate diet the resistance may become very high,—as great as 300 mm of H_2O. Usually, the pressure in the gall-bladder is about 100 mm of H_2O during fasting. After food there is immediate lowering of the sphincter resistance and strong contraction of gall-bladder starts. During contraction of gall-bladder the pressure may be raised to about 250 mm of H_2O.

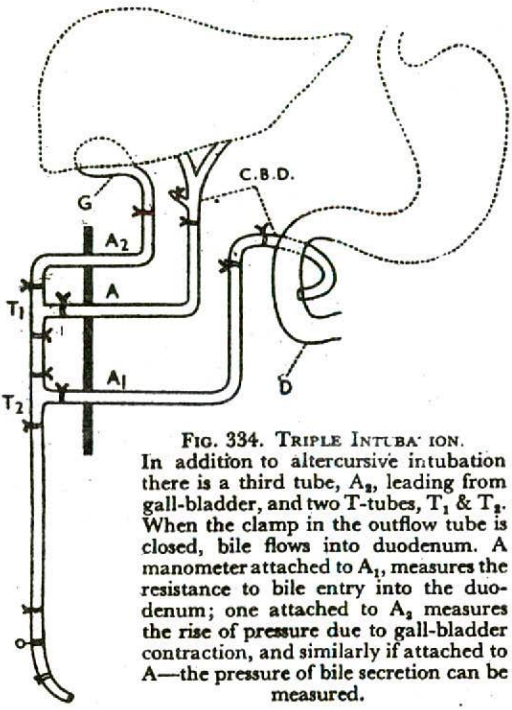


FIG. 334. TRIPLE INTUBATION. In addition to altercursive intubation there is a third tube, A_2, leading from gall-bladder, and two T-tubes, T_1 & T_2. When the clamp in the outflow tube is closed, bile flows into duodenum. A manometer attached to A_1, measures the resistance to bile entry into the duodenum; one attached to A_2 measures the rise of pressure due to gall-bladder contraction, and similarly if attached to A—the pressure of bile secretion can be measured.

Once expulsion starts, it goes on intermittently at frequent intervals for the next few hours as long as digestion and absorption continue. After this, expulsion ceases.

Mechanism. It is obvious that for expulsion of bile two things are required: (1) **increased pressure of bile,** (2) **relaxation of the sphincter of Oddi.** Increased pressure of bile can be brought about by (*a*) *increased rate of secretion of bile,* (*b*) *contraction of gall-bladder.* This latter is brought about by stimulation of the vagus (both conditioned and unconditioned reflexes), high fat and protein diet, cholecystokinin and salts like magnesium sulphate, calomel, etc. Relaxation of the sphincter is also brought about by the same factors (*vide* under 'Movements of Gall-bladder'). From these facts it will be obvious that expulsion of bile takes place only during digestion and absorption of food. This is due to the fact that it is during these processes that the various factors, which stimulate contraction of gall-bladder and relaxation of the sphincter, come into operation.

Factors controlling movements of gall-bladder. Control of gall-bladder seems to be due to two factors: (1) **reflex,** (2) **chemical.**

Reflex control of gall-bladder. Gall-bladder is richly supplied with the vagus and the sympathetic. Stimulation of the vagus causes contraction of gall-bladder and relaxation of the sphincter of Oddi. It is seen from the experiments of Johnson and Boyden that the right vagus carries motor fibres to the gall-bladder and inhibitory fibres to the sphincter of Oddi. Stimulation of the sympathetic exerts opposite effects (Conflicting results have been found by different observers). It is believed that during digestion reflex stimulation of gall-bladder occurs. The stimulus for the reflex may arise in the mouth during eating or due to the presence of food in the duodenum and probably also in the stomach. It has been shown that entry of acid into the duodenum reflexly stimulates contraction of gall-bladder and relaxation of the sphincter of Oddi. It is possible that magnesium-sulphate solution also acts by mobilising this reflex. When introduced into duodenum it causes tonic contraction of gall-bladder and relaxation of the sphincter. Taste or smell of food due to psychic influences causes contraction of gall-bladder.

Chemical control of gall-bladder. (1) **Effect of foodstuffs**—Fatty foods, particularly cream, egg-yolk, etc., are the most effective stimuli. Proteins also stimulate but to a less extent. Carbohydrates have no such effect. Acids are also strong stimulants. These factors cause contraction even when the gall-bladder is completely denervated. This shows that they act through some chemical stimulus. Boyden believes that some products of protein and fat digestion are absorbed into the blood stream and stimulate contraction of gall-bladder. (2) **Cholecystokinin**—Ivy and Oldbergh have shown that acid extracts of duodenal mucosa (as well as from the upper part of the small intestine) can stimulate strong contraction of gall-bladder. The active substance is called *cholecystokinin*. They believe that the active contraction of gall-bladder during digestion is due to the absorption of cholecystokinin.

Action of drugs. Adrenaline, histamine pitressin, etc., stimulates the smooth muscle of the gall-bladder, whereas morphine, ergotamine, atropine, etc., are inhibitory.

Functions of gall-bladder

Functions of gall-bladder can be summarised as follows: (1) It is an **efficient storehouse of bile.** (2) It **absorbs water** and **concentrates bile about 10 times.** (3) It **absorbs inorganic salts** from bile to some extent and **reduces the alkalinity of liver bile.** (4) It **excretes cholesterol** to some degree. (5) It **secretes mucus,** which is the main source of mucin in bile. (6) It **helps in equalisation of pressure** within the *biliary duct system.*

MECHANISM OF SECRETION OF SUCCUS ENTERICUS (INTESTINAL JUICE)

Experiment. The process has been studied extensively in animals. Some informations have been derived from human subjects by collecting succus entericus from small intestinal fistula resulting from war injuries (Savitsch). In animals the experiment is carried out by establishing (*i*) **Thiry fistula,** (*ii*) **Thiry-Vella modification** and (*iii*) **Mann-Bollman fistula.** With the construction of original Thiry fistula, the distal end of the isolated loop was brought to the surface and the proximal end was

closed by suture and left with the abdomen. In Thiry-Vella modification (FIG. 335), operation about 25·4 cm (10 inches) of the small intestine is isolated, keeping blood vessels and nerves carefully preserved. The continuity of the bowel is restored by stitching up the two cut ends of the small intestine. The two cut ends of the isolated loop are sutured to two openings in the abdominal wall. *The aavantage of this preparation is that pure intestinal juice, unmixed with food, can be collected from this loop* and *to allow the loop to be washed through with saline.* The *first two methods lead to the continual loss of* H_2O *and electrolyte.* In the *Mann-Bollman fistula* the distal end of the isolated loop is anastomosed to any desired point in the intestine, and the proximal end is brought to skin surface. Here the secretion of isolated loop is normally passed in the intestine, and dehydration is avoided.

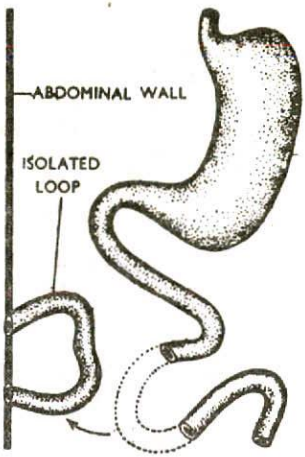


FIG. 335. Thiry-Vella modification.

From such studies, it is seen that very little secretion of succus entericus takes place during fasting. The flow starts about one hour after a meal. During the first two hours the rate of secretion is slow, but it increases in the third hour, persists for some time at a high level and then, as intestinal digestion and absorption are completed, the rate gradually declines and finally ceases.

Mechanism. When the Thiry-Vella loop is mechanically stimulated by introducing a drainage tube, the loop is found to secrete. *It takes place even when the vagi dre cut, but is abolished when the local plexuses are paralysed.* Thus it is obvious that the **mechanical stimuli** work through the local nerves (Meissner's plexus). Under normal conditions, presence of food in the intestine sets up the mechanical irritation which reflexly stimulates the secretion of succus entericus through local nerves.

Vagal stimulation or **injection of acetylcholine** or **pilocarpine** stimulates secretion of succus entericus. On stimulation of sympathetic (splanchnic) nerves secretion of succus entericus is inhibited, but cutting the nerves results in a marked increase of secretion. This secretion, known as **paralytic secretion,** is increased by physostigmine and inhibited by atropine. It is therefore dependent upon some cholinergic mechanism in the intestine. In general, **parasympathomimetic drugs** increase paralytic secretion and **sympathomimetic drugs** tend to inhibit it.

It is found that **products of digestion** of some foodstuff—particularly proteins, stimulate secretion of succus entericus, even when the parts are completely denervated. It is, therefore, a chemical effect. [Food, therefore, stimulates in two ways—*first*, by mechanical irritation and *secondly*, by chemical means.]

Enterocrinin. Nasset and his associates have discovered the presence of a hormone in the intestinal mucosa which when injected stimulates intestinal secretion even when all the nerves are severed. This hormone is called *enterocrinin*. Presence of a second hormone in crude enterocrinin preparation has also been suggested responsible for the release of intestinal enzymes.

Mechanism of secretion of Brunner's gland

Separate regulatory control, both chemical and nervous, exists for Brunner's gland. Vagal stimulation increases the secretion while the chemical (hormonal) agent responsible for increased secretion has been named as **duocrinin.** Secretin is a hormone which stimulates secretion, but glucagon also stimulates secretin.

The **colonic secretion** is rich in mucus and aqueous secretion is scantly. Often it is viscous and opalescent. The reaction is alkaline. Aqueous phase is reabsorbed which is predominant here and the secretion becomes more viscous. The secretion is reflex in nature. The centre is situated in the lumbar spinal cord. The vagi supply the proximal colon, and stimulation produces increased secretion. On the other hand, stimulation of the sympathetic diminishes secretion.

The **appendix secretes** a significant volume of fluid spontaneously or in response to pilocarpine in man, rabbit and chimpanzee. Its secretion is drained freely and continued indefinitely. But if lumen is obstructed, there is a rise in intraluminal pressure and focal ischaemic necrosis occurs, followed by rupture and may lead to infection in this area. Remedy lies in appendicectomy.

Interactions of gastro-intestinal hormones (FIGS. 323 & 329)

As **gastrin** stimulates acid secretion, it probably combines with specific receptor sites on the effector cells. When the concentration of gastrin is high, many receptor sites are occupied and when this concentration is low, few receptor sites are occupied. This relationship between receptor sites and hormones is dynamic.

Cholecystokinin and **gastrin** have the competition for binding on the same receptor of the secreting cell due to the presence of same C-terminal sequence in them (active group), so they have same spectrum of activities. One inhibits the other as competitive inhibition of enzymes and the exhibition of the action of hormone will be noted whose concentration is higher than the other.

Gastrin along with cholecystokinin are additive in stimulations of the pancreas and each of these potentiates the stimulating effect of secretin.

Secretin does not possess the same structure as that of gastrin and cannot inhibit histamine-stimulated acid secretion. When secretin exerts its inhibitory activity on acid secretion, it combines with closely related, but different, receptor site and hence is non-competitive.

During inhibition of acid secretion and motility by secretin, the **pepsinogen secretion** is greatly stimulated. Cholecystokinin and secretin does not inhibit pepsinogen secretion.

The inhibitory action of *chyme* in the duodenum upon acid secretion was attributed to *enterogastrone*. But when the existence of cholecystokinin (pure) and secretin was proved, much of the action of enterogastrone was observed to be a property of these two hormones. All the inhibitory activity of acid in the duodenum is the inhibitory action of secretin. A rapid fall in the histamine-stimulated acid secretion is due to the presence of fat in the duodenum, but not the property of cholecystokinin or secretin. Therefore, it may be presumed that there is another hormone to be isolated. Moreover, the nervous reflex action mediates some of the inhibitory effects of fat and acid.

Metabolic effects of gastro-intestinal hormones (FIG. 329)

In the gastric and duodenal mucosa of rats it is proved that **gastrin** and **pentagastrin** stimulate the synthesis of protein. *Hyperplasia* of the gastric mucosa is the cause of prolonged administration of pentagastrin only in the increased content of parietal cell. Cholecystokinin possesses a similar trophic effect upon the pancreas.

A smaller rise in blood sugar concentration and a prompter increase in plasma insulin content are the effect of glucose absorption from the small intestine than its intravenous administration of an equivalent dosage. Hence this difference proves that there is a role of gastro-intestinal hormones in the metabolic effects. The release of insulin from the β-cells of the islet of Langerhans is stimulated by gastrin, cholecystokinin and secretin and in addition the effect of rising blood glucose concentration in releasing insulin is enhanced by circulating secretin.

Adenyl cyclase activity and **lipolysis in the adipose tissue** are stimulated by secretin and glucagon due to their similar structure. In these respects, secretin is more potent than glucagon.

SUMMARY OF MECHANISM OF SECRETIONS OF THE VARIOUS DIGESTIVE JUICES

SALIVARY SECRETION. Purely a reflex process; two types of reflexes present: **conditioned** and **unconditioned.** Conditioned reflex is proved by the fact that even sight and smell of food stimulate secretion. Other conditioned stimuli can be established. The stimulus for unconditional reflex arises chiefly in the mouth. But it also arises from the oesophagus **(oesophago-salivary reflex),** from the stomach **(gastro-salivary reflex),** as well as from other viscera such as gravid uterus.

GASTRIC SECRETION. [**Experiments**—(1) **Sham feeding.** (2) **Pavlov's pouch.**] **Three phases:** (1) **cephalic** (or nervous), (2) **gastric,** and (3) **intestinal.** (1) **Cephalic phase** starts immediately after taking food. It is a *reflex process involving both* **conditioned** and **unconditioned reflexes.** The juice secreted is called *appetite juice.* It is constant in composition and does not vary with the nature of food. In man it is small in amount but is important. (2) **Gastric phase** starts half an hour after the entry of food in the stomach. The stimulus is chemical. The chemical substance is manufactured by the pyloric mucous membrane from some products of protein digestion and is known as **gastrin.** Gastrin enters blood stream, carried to the gastric glands and stimulates their secretion independent of all nerves. Largest quantity of gastric juice is secreted during this phase. This part of gastric juice varies in quality and quantity with the nature of food. Proteins increase both the amount and the HCl content. Fats inhibit both. Bread stimulates a secretion having the greatest digestive power. Water, coffee, spices stimulate. (3) **Intestinal phase** starts when food enters the duodenum. It is small in amount and is independent of nerves; consequently, the stimulus is chemical but its exact nature is not known. Presence of fat in the duodenum inhibits gastric secretion. This, according to Ivy, is due to the liberation of an inhibitory hormone from the intestine called **enterogastrone.**

The three phases are closely interrelated. Cephalic phase initiates appetite juice, which digests the proteins partly. From these products of digestion gastrin is manufactured which initiates the second phase. After this when gastric digestion has proceeded to the required stage, stomach empties into duodenum and thereby intestinal phase starts. Thus each phase initiates the next.

Even in fasting condition stomach secretes at the rate of 10–60 ml per hour. Its cause is not known. It acts as an antiseptic against *pathogenic bacteria* that may be swallowed with saliva in empty stomach.

PANCREATIC SECRETION. Two phases: (1) **nervous,** and (2) **chemical.** (1) **Nervous phase** starts 1–2 minutes after taking food. *The reflex is purely unconditioned.* Unlike gastric juice there is no conditioned reflex here. The stimulus for this secretion arises both in the mouth (during chewing) as well as from the stomach after the food is swallowed. (2) **Chemical phase** starts when stomach empties into duodenum. This is due to hormone-like substances **called secretin** and **pancreozymin.** Secretin thus enters blood stream, goes to **pancreas and stimulates** the secretion. The secretin fraction

stimulates the secretion of water, alkali and other salts of pancreatic juice; whereas, pancreozymin increases the enzyme content. On the whole, juice stimulated by secretin is rich in alkali but poor in enzyme. Whereas secretion produced by the stimulation of the vagus, is poor in alkali but rich in enzyme. Pancreatic secretion varies with the type of food. Meat stimulates a 'secretin' type of juice, fat stimulates the 'vagus' type; whereas, bread elicits a mixed type of secretion.

BILE SECRETION. [Experiments—(1) Altercursive intubation, and (2) Triple intubation.] Bile secretion by liver is active and continuous, total amount 800–1,000 (15 ml per Kg body weight) per day. The rate of secretion increases one hour after taking food, remains high for 2–5 hours and then falls. At the end of intestinal digestion it comes to the fasting level. The mechanism involves *only chemical stimuli*, nerves are of no practical importance. The chemical stimuli are the following: (1) **Bile salts—chief** cholagogues. (2) **Foodstuffs**—fats and proteins stimulate. It has been noted that bile secretion increases about one hour after meal, remains high for about 2–5 hours and then declines. (3) **Humoral**—Cholecystokinin which stimulates bile secretion by contraction of gall-bladder and hepatocrinin which stimulates the liver cells to secrete bile.

SUCCUS ENTERICUS. [Experiment—Thiry-Vella fistula.] During fasting, no secretion. Flow starts one hour after food, maximum in the third hour, then gradually declines. Mechanism involves two factors: (1) **mechanical,** and (2) **chemical.** (1) **Mechanical factor**—When the mucosa is mechanically irritated secretion takes place. It is independent of the vagus and the sympathetic (splanchnic) but depends upon local nerve plexuses. Presence of food in the intestine acts as a normal stimulus. (2) **Chemical stimulus**—(*a*) **some products of digestion,** particularly of proteins, (*b*) **enterocrinin,** and (*c*) **duocrinin** which acts on duodenum only. All three independent of nerves, act as important stimuli in the normal process of secretion of intestinal juice. Enterocrinin is a hormone manufactured by intestinal mucosa which is believed to act as important stimulus in the normal process of secretion of intestinal juice. It is obvious that all these factors only operate so long as intestinal digestion and absorption continue. Consequently, after this period—(normally 2–5 hours)—the flow will cease.

HUMORAL MECHANISM OF SECRETIONS IN THE GASTRO-INTESTINAL TRACT

The various humoral (chemical) factors controlling the different secretions in the gastro-intestinal tract may be summarised as follows:

I. **For gastric secretion.** (1) **Gastrin**—responsible for gastric phase. (2) **A chemical substance** may be a hormone or secretagogue—responsible for intestinal phase. (3) **Enterogastrone**—inhibits gastric secretion.

II. **For pancreatic secretion.** (1) **Secretin**—main chemical stimulus. (2) **Pancreozymin.** (3) **Foodstuffs.**

III. **For succus entericus.** (1) **Products of protein digestion.** (2) **Enterocrinin**—probably chief stimulus. (3) **Duocrinin.**

IV. **For bile secretion.** (1) **Bile salts**—chief stimulus. (2) **Fat** and **Protein food.** (3) **Hepatocrinin** acting on liver cells. (4) **Cholecystokinin**—which stimulates contraction of gall-bladder.

MOVEMENTS OF ALIMENTARY CANAL

Introduction. The presence of muscular tissue in the alimentary canal indicates that some sort of movements must be present in the gastro-intestinal tract. As a matter of fact, the alimentary canal does move, its different parts showing different kinds of movements.

Why should there be movement. If one recollects the chief functions of the digestive tract, such as digestion, secretion, absorption, defaecation, etc., it would be evident that, unless some kind of movement be present in the gastro-intestinal tract, the latter will not be able to perform its functions properly. For instance, movements are necessary to propel the food mass onwards, in order to bring it in contact with the different digestive juices and also for thorough mixing. Movements are also necessary to ensure active circulation through the walls of the gut, so that secretion and absorption may proceed rapidly. Lastly, movements are essential for the

process of defaecation. All these considerations show that movements are essential requisites for the proper functioning of the digestive tract.

The **broad facts** about the movements are given below:

1. **Classification.** There are many varieties of movements, such as *peristalsis, antiperistalsis, mass peristalsis, segmentation, pendular, tonus rhythm*, etc. Functionally, they can be put into two groups: (*a*) **Translatory movements**—These types of movements travel onwards and propels the food mass, viz., *peristalsis, antiperistalsis*, and *mass peristalsis*. (*b*) **Stationary movements**—These movements remain localised and do not move onwards, viz., *segmentation, tonic contraction*, etc. *Translatory movement is present in every part of gastro-intestinal tract but not the stationary movements.*

2. **Cause of movements.** (*a*) Peristaltic and antiperistaltic movements are **neurogenic,** i.e., depending on nerves, (*b*) segmentation or pendulum is **myogenic,** i.e., depending on muscles only.

3. **Relation with degree of activity.** Movements are directly related to the degree of activity of the part. Greater the degree of activity greater will be the variety and rate of movements. Small intestine, being the most active part, shows the maximum varieties of movements.

4. **Characteristics.** Each type of movement has the following characteristics: (*a*) *nature*, (*b*) *frequency* (i.e., its number per minute), (*c*) *rate of propagation* (if it is translatory), (*d*) *cause* (neurogenic and myogenic), (*e*) *functions.*

DEGLUTITION

Deglutition or **swallowing** is probably a reflex phenomenon. Higher centres facilitate this reflex. Once aroused, the **swallowing centre** in the medulla evokes the complete act of swallowing by discharge through six nuclei and the motor neurones. This reflex act occurs in three stages: (*a*) first or *oral*, (*b*) second or *pharyngeal*, and (*c*) third or *oesophageal* (Fig. 336).

First stage. The first stage consists of the passage of material through the oral cavity into the pharynx which is under *voluntary control.* Due to the contraction of the *mylohyoid, styloglossus* and *hypoglossus* muscles, upward and backward movements of the tongue occur and the **bolus of food** which remains on the upper surface of the tongue is thrown back through the pillars of the **fauces** into the pharynx. During this phase mastication ceases and respiration is inhibited reflexly.

Second stage. It consists of passage of bolus from the pharynx into the oesophagus which is reflex process and known as **swallowing reflex.** The contact of food material with the pharyngeal and peripharyngeal structures initiates and completes reflexly the second as well as third stage of deglutition. These reflexes are inhibited and abolished by *cocainisation.*

The soft palate is elevated and the nasopharynx is closed off from the rest of the pharynx. There are elevation and forward movements of the larynx along with the elevation of the hyoid bone. The vocal cords are adducted and there is momentary *stoppage of respiration and speech.* With the entrance of bolus in the larynx, contraction of superior pharyngeal constrictor occurs inducing rapid pharyngeal peristaltic wave (**primary peristaltic wave**) which moves down the pharynx, propelling the bolus in front of it. The walls and structure of hypopharynx are elevated to engulf the oncoming bolus. The oesophagus, which was kept closed, until now by the contraction of cricopharyngeus muscle, relaxes as the bolus

approaches the oesophagus and thus the bolus enters the oesophagus and the pharynx reopens.

Mechanism of protection of airway during the passage of food through the pharyngeal cross-roads. There are four possible outlets from the oral pharynx through which food may be expelled: (*a*) back into the mouth, (*b*) up into the nasopharynx, (*c*) forward into the larynx, and (*d*) downward into the oesophagus. The swallowing reflex is so co-ordinated that food passes only in one of these possible paths, namely into the oesophagus. Return in the mouth is prevented by the high pressure (even 100 cm of H_2O) developed in this area (posterior half of oral cavity) due to forceful contraction of the tongue against hard and soft palates. Combined actions of tensor veli palatini and levator veli palatini muscles stiffen the soft palate which presses against posterior pharyngeal wall and passage into nasopharynx is prevented. Entrance of food into the respiratory tract is prevented by inhibition of respiration.

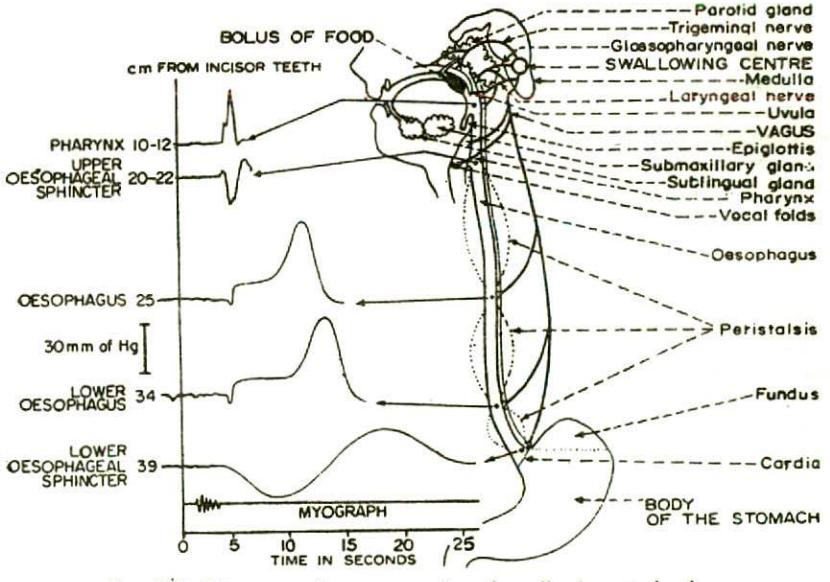


FIG. 336. Diagrammatic representation of swallowing mechanism with pressure changes in the pharynx and oesophagus.

The mechanism of protection of the larynx during the passage of bolus has been the subject of controversy and much study. But it is agreed that the epiglottis is carried into horizontal position by the backward movement of tongue and forward movement of larynx and these movements result drawing up of larynx under the base of the tongue where it is completely out of way of oncoming bolus.

Third stage. It consists of passage of bolus through the pharyngo-oesophageal junction (i.e., upper oesophageal sphincter), body of the oesophagus and oesophagogastric junction (i.e., lower oesophageal sphincter). The terminal part of the second stage and the first part of third stage cannot

be differentiated, because both are same and one. The upper oesophageal-sphincteric mechanism is dealt here along with remaining portion of the third stage. **Upper oesophageal sphincter** is 4 cm in length and usually is located between 15 and 20 cm from the incisor teeth in the region of cricopharyngeus muscle at the level of cricoid cartilage which is characterised by a short zone of high intraluminal pressure (basal-resting pressure 20 to 30 cm of H_2O above the atmospheric pressure). Immediately after the onset of deglutition there is brief increase in the high resting pressure (lasting only a few tenths of a second) followed by marked fall below the resting pressure and there is simultaneously rise of pressure in the pharynx due to arrival of peristaltic wave caused by contraction of the superior and middle pharyngeal constrictor. Thus considerable pressure gradient forms from the pharynx across the sphincter. As soon as the bolus reaches the sphincteric junction the previously relaxed fibres of the upper sphincter contract and propagate the peristaltic contraction and pressure gradient into the upper oesophagus. The positive pressure wave (maximum 70–90 cm of H_2O above the atmospheric pressure) represents a continuation of the pharyngeal peristalsis through the upper sphincter. The pressure within the junctional area then returns to its previous resting basal level within 3–4 seconds.

Body of the oesophagus. The **primary peristaltic contraction** originating in the pharynx already mentioned passes over the pharyngo-oesophageal junction and continues into the oesophagus driving the bolus onward maintaining the pressure gradient. The pressure pattern of this contraction consists of an initial negative wave followed by three positive pressure components. **Secondary peristaltic contraction** also appears in the oesophagus as a result of distention of its wall due to bolus (local) which progresses down like the primary peristaltic contraction and the pressure wave produced by this contraction is similar to final pressure wave of the swallowing pressure pattern. **Tertiary oesophageal contraction** has also been observed which occurs irregularly and locally and is observed in the lower oesophagus mainly.

Lower oesophageal sphincter. Although there was confused idea regarding the terminal few centimetres of oesophagus but it is agreed today that distal 2–5 cm of oesophagus possess a characteristic motor function: (*i*) Deglutition pressure pattern observed in the oesophagus does not propagate into this area. (*ii*) Body of oesophagus and its terminal part react reciprocally to cholinergic and anticholinergic stimulation. (*iii*) High pressure zone is extended from 1–2 cm below the hiatus to 1–2 cm above the hiatus of diaphragm. (*iv*) Mean resting maximum pressure in this region was greater than the pressure in the fundus of stomach is 10·7 cm of H_2O at the end of expiration and 3·5 cm of H_2O at the end of inspiration.

As the peristaltic contraction in the body of oesophagus progresses and approaches the lower oesophagus, the lower oesophageal sphincter relaxes like the cricopharyngeus muscle at upper oesophageal junction and the pressure gradient between the lower oesophagus and lower oesophageal sphincter is formed so that oesophageal content is emptied into the sphincteric area. Then the sphincteric area contracts slowly and the sphincteric content is emptied into the stomach.

Common disturbances in the swallowing

In the first stage. Inflammation of any oral structure, paralysis of tongue and congenital defects of oral structure result difficulty of swallowing.

In the second stage. Acute pharyngitis, tonsillitis, poliomyelitis, diphtheria result difficulty in deglutition.

In the third stage. Diffuse spasm in the oesophagus producing dysphagia and cardiac pain, achalasia (lower sphincter does not relax)-scleroderma (lower part of oesophagus generally in spasm), chalasia (lower sphincter remain relaxed condition, inducing gastro-oesophageal reflux.

Nervous mechanism. The *afferent* impulses reach the swallowing centre through the glossopharyngeal and trigeminal nerves and internal branch of the superior laryngeal, recurrent laryngeal and oesophageal branch of the vagus. The *efferent* nerves are trigeminal, facial, vagus and hypoglossal which regulate the actions of pharynx, larynx and oesophagus musculature.

The **movements of the important parts of the gastro-intestinal tract** are briefly described below.

MOVEMENTS OF STOMACH

Types of movements of the stomach. The volume of chamber of the stomach of a fasting man is about 45–50 ml. Tension in gastric wall is little or nothing and the intra-abdominal pressure is equal to the intraluminal pressure. Movement of its body muscle cannot be seen by X-ray. When a small balloon or an open-tip manometer is placed, pressure changes reflect contraction of the antral muscle at the rate of 3 per minute.

Empiric classifications. Three types of pressure waves are traced from the digestive tract (Fig. 337). Type I waves last 5–20 seconds and are simple monophasic waves of low amplitude, about 3–10 mm of Hg.

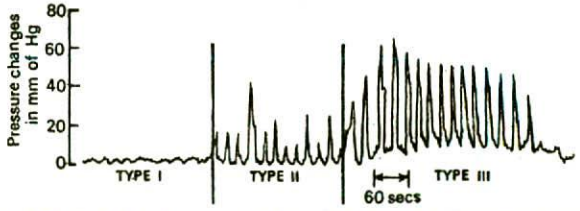


Fig. 337. Graphical representation of three types of pressure waves recorded from the digestive tract.

Type II waves are simple waves of greater amplitude than type I, 8–40 mm of Hg and last 12–60 seconds. In the stomach their rhythmic variation is the same as type I, but in the colon they are about 2 per minute. Type III waves are complex and the rise is less than 15 mm of Hg in the stomach and about 20–30 mm of Hg in the small intestine. Each wave of type III lasts about 1 minute.

Methods of study. It can be studied in animals by opening the abdomen and noting the movements directly. **In man** it can be studied by introducing into the stomach a rubber tube with a balloon attached to its inserted end. The balloon is inflated afterwards. During contraction, pressure changes occur in the balloon which are recorded in a manometer attached to the tube. The inner wall of the balloon may be coated with barium to make it opaque to X-rays, so that its change of shape can be directly watched under X-ray along with pressure changes. It can also be studied directly during operative procedures requiring opening of the abdomen.

From such studies it is seen that the fasting stomach shows a different kind of movement than full stomach. They are briefly described below.

In empty state. In the fasting condition three types of movements are seen in the stomach: (1) **Type I contraction** or **tonus rhythm**—Rhythmic variations of tone occur at the rate of about 3 per minute. (2) **Type II contractions** or **hunger contractions**—At intervals, a series of strong contractions occur involving the whole stomach and lasting for about 30 seconds. Since these contractions are associated with the sensation of hunger, they are called *hunger contractions*. **Type III contraction** is also known as an **incomplete tetanus.** They are usually observed at the end of a period of gastric motor activity and are followed by a period of quiescence. They occur rarely in man.

After a meal. Two different kinds of movements are seen in two halves of the stomach after the entry of food into it. It can be studied best under X-ray after barium meal. The pyloric part has a different kind of movement than the fundus and body of the stomach. Three kinds of movements occur in the **full stomach:** (1) peristaltic waves, (2) systolic contractions of the terminal antrum, and (3) diminution in the size of the fundus and body.

Movements of the fundus and body. A **peristaltic wave** follows the basic electrical rhythm (B.E.R.) of stomach. It starts in the longitudinal muscle of greater curvature as a pacemaker and passes over the body, antrum and pylorus at a rate of 3 per minute and the frequency and rate of progress are influenced by nervous and humoral factors. Rate of progress is 1 cm per sec. in the muscle of body and the duration of wave at a point is 1·5 sec. which is accelerated in the antrum to 3–4 cm per sec. The excitative wave spreads from longitudinal to circular muscle. Consequently irregular band of contraction, 2 cm wide, moves as excitation wave over the body and the antrum following B.E.R. The wave deepens as the digestion proceeds and duration of wave increases.

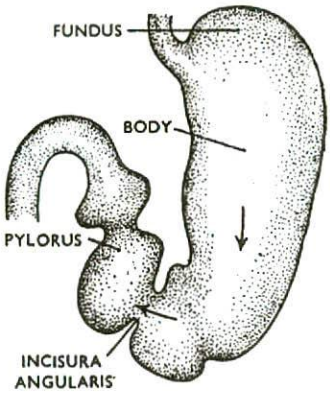


FIG. 338. Constriction waves are seen on both sides of the incisura, passing towards the pyloric sphincter.

Movements of pylorus. The terminal antrum and the pylorus contract with the arrival of wave in their region known as **systolic contraction.** Due to the viscous property of gastric contents and pressing of gastric contents into the terminal part of antrum by the peristaltic wave, the antral pressure rises which overcomes the pressure barrier in the pylorus and thus antral contents passes into the duodenum. The passage of chyme into the duodenum is stopped suddenly by the contraction of pylorus. Since the contraction of last antral portion continues and the pressure rises to about 10–25 mm of Hg, the antral contents are forcibly moved in oral side and not in aboral side, i.e., in the stomach, as the pylorus (pyloric sphincter) prevents it. Thus the reflux of chyme helps in mixing the food with gastric juices. Finally the terminal part of antrum and pylorus relax and continue to relax till the next peristaltic wave reaches the antrum.

Cause of the movements. Excised and isolated stomach when placed in the warm saline, shows rhythmic movements. These contractions are believed to be myogenic because they occur even after the complete division of all nervous connections. However, the present state of knowledge indicates that although the movements in the two parts of the stomach may be mostly myogenic in nature, yet the perfect co-ordination between the tonic contraction of the left half and the peristaltic movement of the right half, depends on the integrity of the local nervous system [Auerbach's plexus.]

Role of the vagus and the sympathetic. Stomach is supplied by both vagus and sympathetic. Although they are not essential for the genesis of the gastric movements, yet, they exert profound influence upon them. Stimulation of vagus does not give uniform results. On the whole, the effect depends on the pre-existing tone of the stomach. When the tone is low, vagus causes contraction, when the tone is high—relaxation. The effect of sympathetic stimulation is also not uniform. *It is generally believed that sympathetic inhibits gastric movements and constricts the sphincter, while vagus stimulates movements and relaxes the sphincter.*

Role of hormones and other chemicals. Adrenaline has the same effect as sympathetic. Pituitrin stimulates gastric contractions. Insulin (as well as low blood sugar) increase gastric movements. Enterogastrone inhibits movements. High gastric acidity is generally associated with a hypermotile stomach, whereas low acidity with a hypomotile stomach.

CONTROL OF PYLORIC SPHINCTER

In the fasting condition the pyloric sphincter remains relaxed. When food enters, the sphincter closes. It then opens at intervals. The time of opening varies with different conditions. For instance, with water and liquid diet, the sphincter almost immediately opens; but with a mixed diet the opening starts at least after 15 minutes (average half an hour). The time of opening depends on (*a*) the normal motility of the stomach, (*b*) quality and consistency of the food, (*c*) stage of digestion and possibly some other factors.

pH. The sphincter is regulated by the pH of the gastric and duodenal contents. High acidity on the gastric side opens it, whereas that on the duodenal side closes it. As gastric secretion proceeds the acidity rises and when it goes up to the critical level, the sphincter opens and gastric contents are pushed into duodenum. Entry of acid chyme in the duodenum raises the acidity of the duodenal contents, consequently the sphincter closes. Thus it goes on alternately, till the stomach is empty. But this view cannot be accepted as a whole. Since, people suffering from achylia, do not show absence of normal activity of pyloric sphincter in general.

Intraluminal pressure. According to some physiologists, opening of the pyloric sphincter depends on adequate pressure. When the peristaltic wave in the pylorus becomes sufficiently strong, the sphincter is forced to open and thus stomach empties into the duodenum. On the other hand, when the antiperistalsis in the duodenum becomes strong, the sphincter is also opened and duodenal regurgitation takes place. Although this view is widely accepted, yet it is seen that in those subjects whose pylorus has been excised the sphincter behaves almost normally.

Amino acid, glucose, fat or fatty acid concentration. The proteose-peptone concentration of the gastric content is supposed to control

the sphincter. As gastric digestion proceeds, the proteose-and-peptone concentration rises and when it arrives at a certain level, pylorus opens. Some quantity is thereby expelled into the duodenum and thereby fall in concentration of proteose-peptone closes the sphincter. After some time the concentration rises again due to further protein digestion and the cycle repeats. Similar reaction of sphincter is seen in case of glucose but reciprocal reaction occurs in case of fat or fatty acid.

Osmotic pressure. The osmotic pressure of the gastric content is another factor that controls the sphincter. When the osmotic pressure of the gastric content approaches that of the saline constituent of the plasma, the sphincter opens. As digestion proceeds, number of dissolved particles increase, so that osmotic pressure rises. When it goes up to the requisite level, the sphincter opens.

Tonus. Gastrin increases tonus whereas enterogastrone or urogastrone inhibits tonus, so intraluminal pressure increases and decreases respectively.

It may be concluded that the opening and closure of the pyloric sphincter depend on several factors.

EMPTYING OF STOMACH

The type of foodstuffs and their consistency determine the emptying time of stomach. Water almost immediately passes out, liquid food is emptied more rapidly than solid. Larger meals have necessarily longer emptying time. A small amount is being evacuated out at an interval of every 20 seconds. The emptying of the stomach is regulated by the accumulation of evacuated substances in the intestine. Fats are retained or the longest time, because they inhibit gastric movement. Fats act through the hormone, enterogastrone released into the blood from the mucous membrane of the intestine. Carbohydrates leave early. Proteins are intermediate. Products of protein digestion act mainly through the vagi—**enterogastric reflex.** In animals mechanical irritation or distention of the duodenum is followed by inhibition of peristalsis and this is due to enterogastric reflex mediated also through the vagi. *With a normal mixed diet the stomach completely empties in about three and a half hours. With a rich fatty diet about four and a half hours.*

VOMITING (EMESIS)

Definition. *Vomiting is a reflex which serves to relieve the upper G.I. tract by forcible expulsion of gastric contents through the mouth.* This may occur either because the contents are irritating or because the organs themselves or the nerves that supply them are more irritable than normal. Excessive distention and compression or irritation of the intestine, appendix, bile ducts and other abdominal viscera can also initiate this movement. This is a reflex movement (FIG. 339).

Sequence of events. A number of events takes place during vomiting, more or less, in the following order:

1. **Nausea.** At the onset a feeling of nausea is experienced, followed by excess salivation.
2. **Glottis becomes closed and the nasopharynx is also shut off by raising the soft palate.** The purpose is to prevent the entry of any vomited material into the trachea and nose.
3. **The body of the stomach, the cardiac sphincter and the oesophagus relax.** The pylorus contracts and presses its contents into the relaxed stomach. Weak contraction and antiperistalsis may take place in the stomach but they are not important, because vomiting normally takes place even if stomach is replaced by a bladder. Pyloric sphincter remains closed.

4. **Intra-abdominal pressure sharply rises.** This is caused by retching during which expiratory muscles, abdominal muscles and diaphragm contract. These contractions increase the intra-abdominal pressure so that the relaxed stomach is forcibly compressed. This increased intra-abdominal pressure is the chief motive force of vomiting. Gastric contents

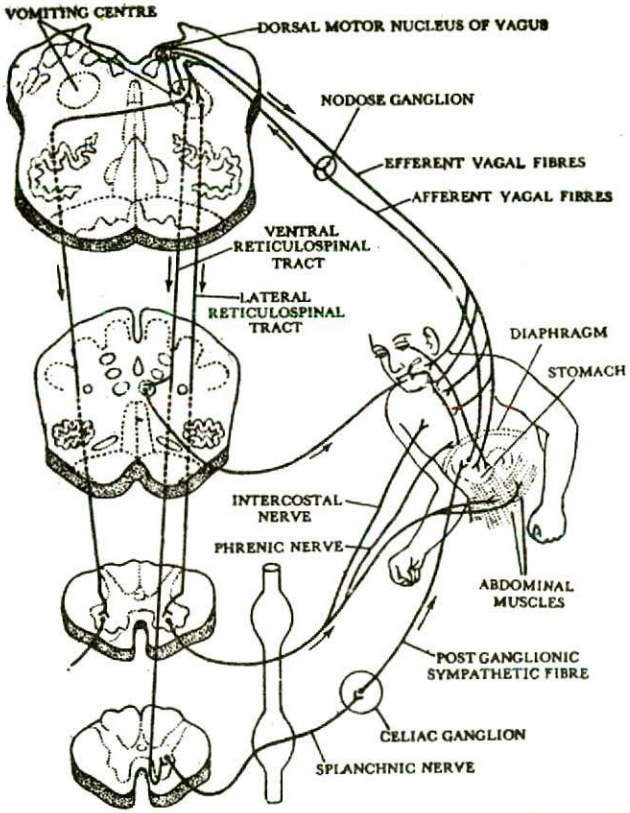


FIG. 339. Vomiting reflex. Diagram showing viscerovisceral and viscerosomatic reflexes initiated from irritation of the stomach, the afferent impulses being carried in the vagus. The actions involved are: (*a*) elevation of soft palate, (*b*) larynx and hyoid drawn forward, (*c*) salivation and opening of mouth, (*d*) closure of glottis, (*e*) relaxation of oesophagus, (*f*) opening of cardia, (*g*) flaccid relaxation of stomach, (*h*) constriction of lower end of stomach, (*i*) inhibition of normal respiration, (*j*) forced inspiration, (*k*) sharp, spasmodic contraction of diaphragm and abdominal muscles, (*l*) characteristic posture—flexion of waist, clenched fists, etc.

are pressed into oesophagus and then from the latter ejected out through the mouth. Antiperistalsis may take place in oesophagus helping ejection.

5. **The process continues till the stomach is empty.** Towards the end diaphragm ascends (relaxes) and the expiratory muscles contract. Glottis being closed it raises the intrapulmonary pressure and compresses the oesophagus. This helps to expel the last remnants of the vomitus from the oesophagus.

Mechanism. *Vomiting is a reflex process.* Straightforward vomiting is governed by a *vomiting centre* which is situated in the dorsal part of the lateral reticular formation of the medulla lying ventral to the solitary tract and its nucleus.

It forms one of the component of the complex visceral centres which include salivation, defaecation and vasomotor centre and vestibular nuclei. So there is consistent relationship of vomiting with salivation, defaecation, respiration and vasomotion. This centre can be *directly* stimulated (central vomiting) by certain drugs (apomorphine, etc.), certain toxins (such as those of uraemia), increased intracranial pressure (brain tumour, asphyxia, meningitis, etc.) and such others. It can be *reflexly* stimulated in various ways.

There are two pathways by which the vomiting centre is affected: (*i*) *nervous path*, and (*ii*) *vascular path*. The nervous path lies in the various afferent pathways coming from various organs especially digestive tract. The most sensitive part is in the first part of duodenum. The *afferent* impulses may also arise in the throat (tickling—sensory nerves V and IX), stomach (irritation), intestine or other organs outside the gastro-intestinal tract like heart, kidney, uterus or semicircular canals.

Chemical substances (emetics) pass *via* body fluids and act on chemosensitive area called **chemoreceptor trigger zone** in the floor of IVth ventricle and cause vomiting. Destruction of this area results loss of response when emetics placed directly on the receptor site in chemoreceptor trigger zone.

The *efferent* impulses—both excitatory and inhibitory, are carried in the phrenic chiefly and vagus and the sympathetic.

The commonest cause of vomiting is gastric irritation and its purpose is to drive out the irritant from the stomach.

Projectile vomiting. The central vomiting caused by stimulation of central nervous system (e.g., trauma and tumour in brain and irritation in meninges, etc.) is projectile type having little feeling of nausea and absence of participation of voluntary muscles.

Persistent type of pernicious vomiting of pregnancy. In this type the excitability of the centre is increased by metabolic disturbances (e.g., carbohydrate starvation and dehydration with ketosis.

Loss of water, and both H^+ and Na^+ ions due to excessive vomiting might be harmful.

Emetics are substances that cause vomiting (such as drinking of sodium chloride and warm water).

MOVEMENTS OF SMALL INTESTINE

The following types of movements are found in the human small intestine: (1) **rhythmic segmentation** or **Ludwig's pendulum,** and (2) **peristalsis.** Each type is briefly described below:

1. **RHYTHMIC SEGMENTATION—Nature.** These are rings of contraction occurring at regular space of intervals in which a portion of the intestine is divided into segments. The contraction is followed by relaxation. The contraction takes place at the site of maximum distention. It can be studied under X-ray after barium meal. The opaque column of barium meal becomes broken into several small segments. At the next moment each of these segments is subdivided by a fresh batch of contractions, the previous group having disappeared in the mean time. The halves of the

adjacent segments so divided run together and form new segments. These are again subdivided and thus the process goes on (Fig. 340). According to Friedman, there are two types of segmenting contractions in the duodenum: (1) One type consisted of a contraction localised in a segment less than 2 cm and was **eccentric** in appearance. (2) The other was **concentric** and consisted of a local contraction involving a segment usually longer than 2 cm and uniform circumferentially.

Frequency. In animals the groups of contractions succeed at the rate of 20–30 per minute. In man the rate is slower. The frequency is inversely proportional to the distance from the stomach. A cyclic changes in the electrical potential occurred in the duodenum known as basic electrical rhythm (B.E.R.) originates near the entrance of the bile duct and moves down the duodenum. In the duodenum it is about 17 per minute, in the ileum it is about 12 per minute. In addition, irregular bursts of spike potential superimposed on B.E.R. appears in an

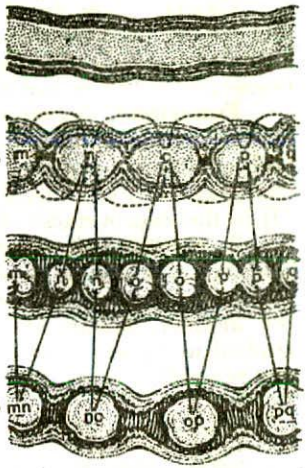


Fig. 340. Diagram representing the process of rhythmic segmentation in a segment of the small intestine and sequence of events from A to D. A quiescent loop of the small intestine in *A*, suddenly divides itself by contraction of its circular muscle fibres in a good number of segments as in *B*. Only after a few seconds each of segments divides into two parts as in *C*. Afterwards each of the halves as *m*, etc., which are formed from previous segments unite with neighbouring halves as *n*, etc., formed from another segment and thus forms a new segment as *mn*, etc. in *D*, of the equal size as the original *B*.

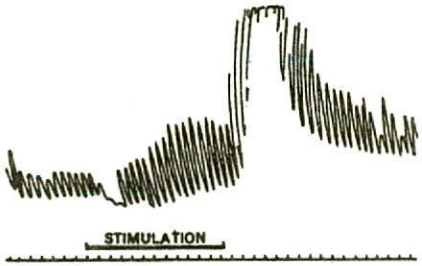


Fig. 341. Tracing representing effect of stimulation of the vagus on intestinal contraction (diagrammatic).

electrical record. So the contraction is segmental and not peristaltic since spike potential and contractions do not proceed more than a few centimetres. The duration of electrical cycle is about 3·5 sec. and hence the rhythm is 17–18 per minute. The frequency variation at different region is due to gradient in the physiological properties, viz., rhythmicity, irritability, variation in latent period and drug succeptibility. Muscular contraction occurs at intervals of some multiple of 3·4 seconds and do not travel very far along the intestine. The vagi (Fig. 341) and the splanchnic

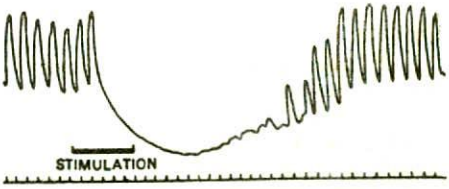


Fig. 342. Graphical representation of effect of stimulation of both splanchnic nerves on intestinal contraction (diagrammatic).

nerves (FIG. 342) regulate the activity of the intestine, and adrenal medulla in psychic conditions, but action of these nerves is reversed in the control of ileocaecal sphincter.

Cause. These are the most fundamental movements of the intestine and are due to outstanding property of smooth muscle that is rhythmicity. Circular muscle is responsible for the most visible movement. They are myogenic in nature and are independent of all nerves.

Functions. *Segmentation movement* does not cause forward passage of food materials. It helps (1) in digestion due to **proper mixing** of food with enzymes of digestive juices, (2) in **absorption** due to (*a*) constantly changing the layer of fluid in contact with mucosa, (*b*) change in pressure, (3) in the improvement of intestinal circulation.

2. **PERISTALSIS—Nature.** *Peristalsis is described to be a composite wave, consisting of a wave of relaxation followed by a wave of constriction. It is a translatory movement and travels down the gut in an aboral direction* (away from the mouth). Bayliss and Starling have demonstrated that a stimulus applied to a given point on the intestinal wall causes contraction above and relaxation below the stimulated point (FIGS. 343 & 344). This is a local reflex of smooth muscles and their intrinsic plexuses. This is called *The Law of Intestine or Myenteric Reflex.* It is suggested that peristalsis depends on this reflex.



FIG. 343. Diagram showing helical arrangement of smooth muscle in the small intestine with longitudinal helix being incomplete and tighter than normal and circular helix being complete.

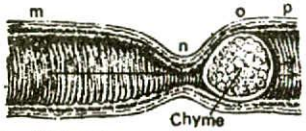


FIG. 344. Diagram showing peristalsis. Due to presence of chyme at *o* a local stimulation is provided making the circular muscle at *p* to relax and at *n* to contract and thus propelling the material down the intestine.

Usually two types of contraction, viz., peristaltic and rhythmic segmenting are present simultaneously, the former is superimposed on the latter and responsible for rise into the tone level of intestinal muscle without any interruption in the rhythm of the segmenting contraction. Peristaltic wave travels for varying distances—some few cms and other a few metres depending on the intensity of stimulus. Segmental contractions sometimes recur frequently maintaining its character and travel aborally as peristaltic movements. A peristaltic wave induced by strong stimulus may sweep over the entire, length of small intestine what is called *rush wave* or *peristaltic rush.*

The peristaltic waves move aborally and not orally and are due to the gradient of rhythmicity, conductivity and irritability. The impulse arises in the most irritable point and travels in the less irritable, i.e., the aboral side and not in the oral side due to the long refractoriness.

Types of peristalsis. Three types of peristaltic movements are present in the small gut: (*a*) **First type** is a slow gentle wave moving at the rate of 1–2 cm per second which dies out easily after travelling a short distance. (*b*) **Second type** is a very swift wave travelling the entire length of small gut at the rate of 2–25 cm (average about 10 cm) per second. According to Alvarez the latter is true peristalsis. Due to its rapid speed it is also known as *rush peristalsis.* (*c*) **Third type (anti-peristalsis).** In every respect it is same as peristalsis excepting that its

direction is opposite. *It moves in the oral direction.* It is present *in the second and third parts of duodenum only* in man. Weak antiperistalsis also occurs in the terminal part of the ileum, thus preventing a rapid passage of the ileal contents into caecum. In the duodenum it helps thorough admixture, as well as causes duodenal regurgitation into the stomach. These antiperistaltic movements occur due to presence of sensitive receptor area in this region which responds to the qualities of chyme and concerned with delaying the passage of chyme into lower portion of the gut facilitating more scope of digestion and absorption.

Cause. Peristalsis depends on both nervous and chemical factors. The vagi and sympathetic have got influence on peristaltic movements. Stimulation of vagus increases and that of sympathetic inhibits peristalsis. Vagotomy on the other hand decrease the peristaltic activity only to a minor extent. The local nerve plexus (Auerbach's plexus) helps in the co-ordination of peristaltic movements. Distention of the intestine, normally caused by presence of food, causes peristaltic movements due to a stretch reflex called **myenteric reflex.** Reflex inhibition of whole of the small intestine may take place due to stretching of lower part of the small intestine (such as intestine and intestinal reflex) or stretching of gall-bladder and urinary bladder, etc. These inhibitions may be removed by stimulation of splanchnic nerves (sympathetic). Presence of local nerve plexus (myenteric plexus) are required for this and the afferent receptors of which are present in the mucous membrane of the intestine. Liberation of 5-hydroxytryptamine (**serotonin**) from the enterochromaffin cells is a possible mediator in this reflex action. Role of a basic polypeptide, **substance P** as a mediator has also been suggested.

Role of endocrines. Hormones also exert great influence. Pituitrin excites the movements, as also thyroxine. Adrenaline inhibits the movements.

Gastro-ileal reflex. This is a special manifestation of peristaltic movements in the ileum. Peristalsis is generally very sluggish in the last part of the ileum. But after a meal, brisk peristalsis is set up reflexly in this region. This is called *gastro-ileal reflex.* The purpose is to drive out the ileal contents into caecum and thus making room for fresh supply.

Functions. (1) **Chief function is the propagation of the food onwards.** (2) Other functions are same as of segmentation movement.

The **metabolic gradient theory** of Alvarez is important in this connection. He observes that excitability, frequency of movement, strength of contraction, tone of the intestine gradually diminish from above downwards along the intestinal canal. Even the normal direction of peristalsis is from above downwards. The latent period of the intestinal muscles gradually becomes longer in the lower parts of the small intestine. This peculiarity, according to Alvarez, is due to the difference in the degree of metabolic activity between the upper and lower parts of intestine. The metabolic rate is much higher in the upper part than in the lower part and it is this gradient upon which this difference depends. In certain pathological conditions of intestine, such as, inflammation, obstruction, etc., the metabolic rate of the diseased part may be higher than those above it. So that under such conditions, antiperistalsis will start at the site of lesion and proceed towards the stomach. This theory explains the phenomenon of faecal vomiting during intestinal obstruction.

Movements of duodenum. It is seen that in the intestine, duodenum is the place, where many peculiarities of movements are seen. It possesses peristalsis and segmentation movements all along. The second and third parts possess the additional movement of antiperistalsis. The first part, i.e., from the end pyloric sphincter to the opening of bile duct, also known as *duodenal cap,* possess special receptive area which responds to the qualities of chyme. It has got its own rhythmicity different from its adjacent parts.

ILEOCAECAL SPHINCTER

The ileum and colon is separated by a barrier called ileocaecal sphincter, situated at the junction of the two, which normally remain closed (Fig. 345). Its functions are to delay the passage of chyme from the small intestine and to prevent regurgitation of material from the colon into the small intestine, thus facilitating more digestion and absorption. Gastro-ileal reflex and enterogastric reflex exert influence of activity in one part of the digestive tract on that of another part. The former reflex results increased motility of last part of ileum and relaxation of ileocaecal sphincter due to incoming of food into the stomach and this ileocaecal content is present in the caecum through the sphincter. The latter reflex results relaxation of stomach due to reaching of chyme into the caecum. The time space is so adjusted by these two reflexes that when food residue of meal reaches into the caecum, the other meal enters into the stomach. The closure of the sphincter is due to the myenteric reflex of caecum which is initiated by mechanical stimulation of the caecal mucosa by the chyme.

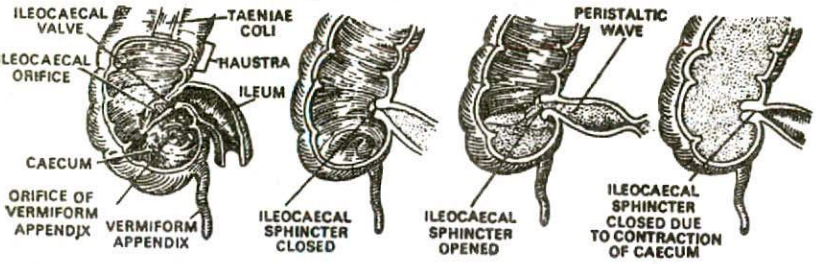


Fig. 345. Diagrammatic representation of ileocaecal valve, after removing the anterior wall of terminal ileum and caecum which prevents regurgitation of caecal contents in the ileum.

MOVEMENTS OF VILLI

Villi possess independent movements of their own. These movements are due to the contraction of strips of muscle fibres which proceed from muscularis mucosae and get attached to the sides of the villus. Generally, *two kinds of movements are seen*: (1) **Side-to-side movement**—In this movement the villi bend to one side which may be in any direction. This is caused by the contraction of muscle strip on that side. The function of this movement is to help admixture and also to help absorption by bringing the villi in contact with different portions of food mass. During active digestion these movements are very rapid. (2) **Pumping movements**—In this movement all the muscular strips around the villus contract simultaneously and the villus shorten in length as a whole. At the height of digestion and absorption this movement takes place at the *rate of about* 1–6 *per minute*. The function of this movement is the increase of flow of blood and lymph.

Beside these movements, the villus performs protecting action on the inflammation due to the contraction of muscularis mucosae as a result of contact of sharp foreign body in the intestinal contents.

Factors controlling movements of villi. (1) **Mechanical irritation** of food acting through the local nerve plexus. (2) **Neural stimuli**—Stimulation of the splanchnic nerve augments the movement of villi. Stimulation of the sympathetic nerves causes contraction of the muscularis mucosae. The nerves are adrenergic and respond to sympathomimetic drugs. The muscularis mucosae also responds to parasympathomimetic agents, e.g., acetylcholine with contraction. They are depressed by atropine and nicotine. (3) **Chemical stimuli**—Some products of food digestion, specially some amino acids, as well as yeast extracts (vitamin B) act as

strong stimulants. (4) **Villikinin**—This is a hormone that can be extracted from the intestinal mucosa. The structure of it is not definitely known but possibly not protein in nature. It is believed that during active digestion villikinin is absorbed through blood and stimulates the movements of villi.

It will be seen from the above that all these factors operate during digestion of foodstuffs. Hence, during digestion the movements of villi are very brisk. During fasting they are very slow.

Movements of villi cease during asphyxia, loss of blood, circulatory failure, etc.

MOVEMENTS OF LARGE INTESTINE

The colon receives mixed residues of food which have escaped digestion and absorption in the stomach and small intestine, i.e., undigested or undigestible food residues, whatever remains of digestive juices including large amount of H_2O and the fluid that has been swallowed or secreted and has escaped absorption in the small intestine in liquid form.

The colon extracts mainly H_2O and other substances to some extent, viz., glucose, amino acids, NaCl and drugs, etc., from this mixture and convert it to a solid form of faecal masses to be evacuated through the anal canal by means of its different movements which may be divided into two classes: (*i*) *stationary* and (*ii*) *translatory*.

1. **Stationary movements.** These are localised movements having no absolute forward movement of masses and are responsible for the agitation of the colonic contents and extraction of H_2O and other substances from liquid mixture of food residues received in the colon which appear to be performed by the four types of movements successively.

(*a*) **Segmenting contraction,** as seen in small intestine, (*b*) **haustral contraction** (bulging of wall of colon between the teniae), (*c*) **kneading movements** (fairly large segment contract while adjacent segment relaxes and followed by contraction and relaxation in reverse phase), (*d*) finally by means of **peristalsis** and **antiperistalsis.** These movements occur principally in the ascending and transverse colon for the maximum absorption of H_2O in this area. Each type of these movements not necessarily occur in every species of animal.

2. **Translatory movements.** The second class of movements includes colonic (*a*) **peristalsis** and (*b*) **mass peristalsis** which propel the colonic contents anal wards. (*a*) **Peristaltic movement** in colon is the same as that of small intestine except in frequency. The power of contraction is greater in the descending colon due to dry and hard character of the material to be moved. In this type of movement, integrity of myenteric plexuses is not required. (*b*) **Mass peristalsis** is also a propulsive nature but is not true peristalsis since it involves simultaneous contraction of large segments of the colon. This occurs generally when the stomach is filled with food (unconditioned) or as reflex process called **gastrocolic reflex** which may be also due to *conditioned stimulus*. This gastrocolic reflex may be preceded by gastro-ileac reflex. This movement serves to empty of the contents of the proximal colon into the more distal portion and finally into the rectum giving rise to feeling or desire to defaecate.

Functions of large intestine

Large intestine serves the following functions:

I. Absorption—1. **Water absorption and formation of stool** is one of the chief functions of large intestine. Daily about 350 gm of fluid chyme is passed into the large gut and about 135 gm of moist faeces is produced on average. About 60–80% of water is absorbed here.

2. **Saline.** Normal saline is freely absorbed.

3. **Glucose.** Isolated large intestine absorbs glucose at the rate of 6 gm per hour. 5% glucose solution is suitable for administration per rectum in the human subject.

4. **Certain drugs,** e.g., some anaesthetics are absorbed.

5. **Amino acids** are also absorbed.

Absorption in the proximal colon is better than in the distal.

II. Excretion—Heavy metals like bismuth, mercury, arsenic, etc., are excreted through the large gut. The diffusible substances present in the bolus may be excreted if the concentration of these substances in the colon is lower than the blood. Due to the basis of which, this part of intestine may be used as **artificial kidney** for removal of body waste product whose kidney is in trouble provided the concentration of these substances in the intestine is kept lowered by withdrawing them from it constantly. When they are injected subcutaneously they appear in the faeces.

III. Secretion—The goblet cells of the large intestine **secretes mucus** which acts as a lubricant. Mechanical irritation stimulates some watery secretion. The secretion of the large intestine has a distinct alkaline reaction (pH 8·4), but normal stool has an acid reaction due to acids produced by bacterial action.

IV. Synthetic functions—Bacterial flora of the large intestine synthesises vitamin K, folic acid and some other members of vitamin B complex. Large amounts of vitamin B_{12} are also synthesised but they are not absorbed.

V. Bacterial digestion—Large intestine is the seat of growth of various types of micro-organisms or bacteria. Whether they are useful or not, is not definitely known. But the following facts indicate that they may be useful to some extent.

These bacteria are very rich in cytochrome. Some observers believe that it is from the dead body of these bacteria that the human body derives a large part of its cytochrome requirement. Some people suggest that the normal flora of the large intestine prevent the growth of other pathogenic bacteria and thus serve a very useful purpose.

In the herbivora, celluloses are digested by the cytases present in the vegetable cells or by the action of bacteria. In human being, cellulose, hemicellulose, etc., form the dietary residue. It has been suggested that some people suffering from chronic constipation can break down cellulose more than normal ones, thus reducing the bulk.

The unabosrbed foodstuffs pass into the large intestine where they are attacked by the bacteria with the formation of products as follows:

(*i*) **Carbohydrates**—are converted to CO_2, organic acids, etc. Cellulose is converted into carbonic acid and methane.

(*ii*) **Fats**—are converted to lower fatty acids and glycerol.

Choline is converted to a toxic product called **neurine.**

(*iii*) **Proteins**—are converted into amino acids, ammonia, etc.

(*a*) By decarboxylation amines are produced:

Histidine ——→Histamine. **Tyrosine** ——→Tyramine.

Lysine ——→Cadaverine. **Arginine** ——→Putrescine.

Putrescine and cadaverine together constitute ptomaine which is said to be responsible for the so-called ptomaine poisoning.

(*b*) By reductive deamination:

Tryptophane——→Indole and Skatole.

Bad odour of the faeces is due to indole and skatole and is called the **bowel breath.**

Tyrosine and Phenylalanine——→Phenol and Cresol, etc.

VI. Movements—One great function of the large intestine is its capacity to move. Its mass peristalsis is essential for defaecation.

RATE OF PROGRESS OF BARIUM MEAL

The barium meal (Fig. 346) starts leaving the stomach almost immediately after it has been swallowed. It passes steadily through the duodenum and *very rapidly through the jejunum, where it may be found after one hour.* In the ileum its progress gradually becomes slower. *It reaches the last part of ileum in about three and a half hours.* By this time stomach should be completely empty. *In the caecum it is found after four and a half hours, hepatic flexure—6–6½ hours, splenic flexure—nine hours, descending colon—eleven hours, ileac colon—twelve hours, pelvic colon—eighteen hours.* Evacuation occurs usually between 16 and 24 hours. The first part of the meal is found in the stool at this time but the last traces may persist normally up to 48 hours. These time relations are important for radiological examination of the gastro-intestinal tract, and also for testing the degree of constipation in the subject. For the latter purpose, the subject is given charcoal biscuits and the time of appearance of charcoal in the faeces and its complete clearing is noted. From this the degree of constipation can be judged.

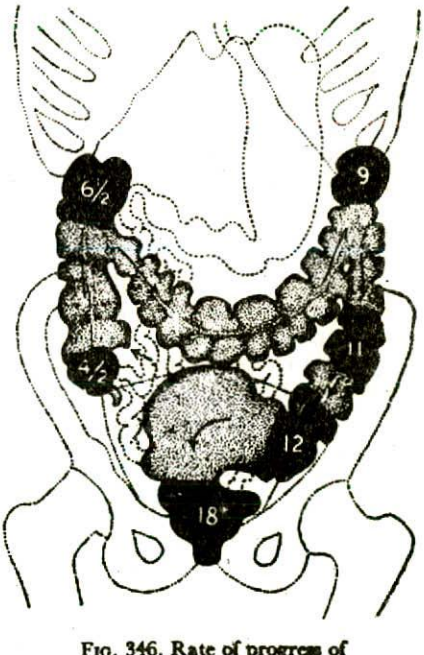


Fig. 346. Rate of progress of barium meal.

DEFAECATION

Defaecation is an act of emptying of entire distal colon from the splenic flexure through the anal orifice into the exterior which is a reflex process. The reflex is initiated by the rise of intraluminal pressure of about 20–25 cm of H_2O in the rectum containing pressoreceptor which not only detects increase of pressure but also differentiates whether the increase in pressure is due to gas, liquid or solid. The reflex centres have been located in the hypothalamus, in the lower lumbar and upper sacral segments of the spinal cord and in the ganglionic plexus of the gut. This is a reflex which is under some degree of voluntary control.

Mechanism. The rectum is normally empty. The faecal matter is stored in the sigmoid and pelvic colon and not in the rectum. As soon

as some faecal matter enters the rectum due to mass movement there is a desire for defaecation along with voluntary effort, e.g., assumption of appropriate posture, voluntary relaxation of external anal sphincter and abdominal compression in the adult, etc., which may further augment visceral reflexes. These reflexes result mass contraction of entire length of colon and relaxation of internal anal sphincter. Thus the colon contents pass into the pelvic colon, rectum, anal canal and finally removed from the body. Defaecation reflex can be initiated earlier or inhibited voluntarily.

DIGESTION OF FOODSTUFFS

Definition. The term **digestion** *may be defined as the process of biochemical transformation of complex and larger food particles in the gut enzymatically into a simple form suitable for absorption and assimilation, the complex and higher molecules being unsuitable for absorption.* If a brief survey is made of the whole process of digestion the following broad facts are seen: (1) There are *four* digestive juices: saliva, gastric juice, pancreatic juice and succus entericus. Bile may be taken as the *fifth* one. (2) Digestion is carried out by enzymes. Various other factors help the enzymes to carry out their functions. (3) Excepting the milk-coagulating enzyme, all the other digestive enzymes perform their functions by a process of hydrolysis. (4) One digestive juice does not possess all the enzymes necessary for the digestion of all the varieties of foodstuffs completely. For this reason, digestion is carried out in 'relays'. One digestive juice digests up to a certain stage, further digestion is carried out by the next one and in this way the process goes on to completion. (5) It should be further noted that simultaneous absorption along with digestion is an essential factor for complete digestion. Because, if not removed by absorption, the end products of digestion will accumulate and set up a reversible enzyme action. Thus complete digestion will not be possible.

The process of digestion of the different types of foodstuffs is briefly described below:

DIGESTION OF CARBOHYDRATES

Introduction. Although dietary carbohydrate is entirely *dispensable* but the diet of most of the countries includes 60–80% carbohydrate and they are eaten mostly as oligosaccharides or polysaccharides and to a lesser extent monosaccharides. Monosaccharides are usually absorbed into the portal vein by the intestinal mucosa so polysaccharides or oligosaccharides should be digested. Daily intake of carbohydrate ranges from 300–800 gm per day in adults which generally supplies 1000 to 2500 calories.

The **different forms** of carbohydrates which are generally included in diet are as follows: (*a*) **Polysaccharides**—*starch, dextrin, glycogen* and *cellulose.* (*b*) **Oligosaccharides (disaccharides)**—*lactose, maltose, sucrose.* (*c*) **Monosaccharides**—*glucose* and *fructose.* Of these types, cellulose containing β-1,4′ linkages cannot be appreciably digested in the human alimentary canal. Monosaccharides need no further digestion, because all carbohydrates are absorbed in the form of monosaccharides. Hence, ***digestion of carbohydrates includes the digestion of polysaccharides and oligosaccharides. Digestion of polysaccharides or oligosaccharides starts in the saliva and is completed in the succus entericus. Digestion of oligosaccharides (disaccharides) chiefly takes place in the succus entericus, but may occur to a slight extent by other digestive***

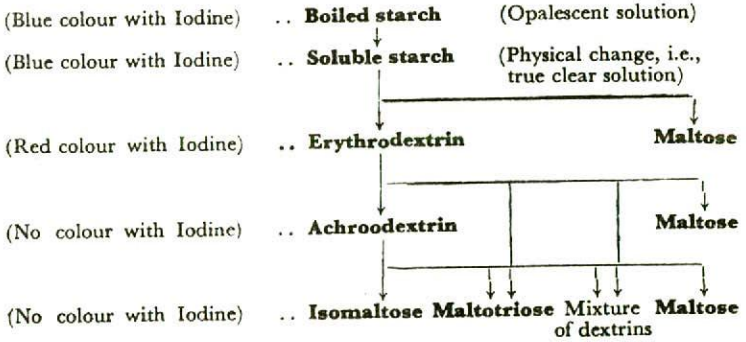
juices. The brief details of the digestion of starch and disaccharides are as follows:

In the saliva. Saliva contains (*a*) chiefly **salivary amylase** or **ptyalin** and (*b*) traces of **maltase** (Its presence in saliva is doubtful). Salivary amylase (α-type) whose origin in the saliva, acts on starch (which is mostly amylopectin type) and contains straight chains held by 1,4′-α-glucosidic linkages and branch chains whose branch points are 1,6′-α-glucosidic linkages. Maltase acts on maltose.

Conditions and peculiarities of ptyalin action. (1) Ptyalin acts on *boiled starch only*. It cannot penetrate the intact cellulose covering of the unboiled starch particle. (2) Optimum reaction is slightly acid (pH 6·5), but it can also act in neutral or slightly alkaline medium. (3) Strong acid (such as HCl of gastric juice) destroys ptyalin. (4) Optimum temperature is about 45°C. At 60°C. it is destroyed. (5) Effects of salts (such as chlorides) are necessary for ptyalin action. (6) Ptyalin digests starch up to the maltose stage only.

Site of ptyalin action. Although digestion of starch starts in the mouth, yet ptyalin action chiefly takes place in the stomach (before the HCl concentration becomes high). On an average it continues for 30–40 minutes. Under favourable conditions, starch is converted into maltose, isomaltose and maltotriose.

Stages of ptyalin digestion. Ptyalin which hydrolises only α-1,4′ linkages but not the α-1, 6′ linkages and splits the more central linkages. α- and β-amylases* supplement each other's action upon amylopectin as β-amylase splits maltose from the end groups and α-amylase splits central linkages to form more end groups. By its action isomaltose (containing 3 glucose molecules in which there is one α-1, 6′ linkages), maltose (glucose-glucose), maltotriose (glucose-glucose-glucose) and a mixture of dextrins (containing the α-1, 6′ branches and averaging six glucose residues per molecule) are produced. The stages are briefly as follows:



In the gastric juice. Gastric juice does not possess any carbohydrate-splitting enzyme, but gastric HCl can carry on some hydrolysis of *sucrose*.

In the pancreatic juice. Pancreatic juice contains two enzymes acting on carbohydrates: (1) **Pancreatic amylase** acting on starch and dextrin. Hopkins has divided the amylases into two groups: α-amylase or

* β-amylase present in vegetable starch and in all germinating seeds.

endoamylase is of animal origin and β-amylase or exoamylase is of plant origin. α-amylase acts on the polysaccharide on the interior of the chain and β-amylase from the non-reducing end. (2) **Maltase** (in traces) acting on maltose.

Conditions of action of pancreatic amylase are as follows: (*a*) *It can act on both boiled and unboiled starch.* (*b*) Its action is much more rapid than ptyalin. Most of the starch is converted into maltose within a few minutes. (*c*) Optimum reaction ranges from pH 6·7–7·0, i.e., slightly acid or neutral. It can also act in slightly alkaline medium. (*d*) Optimum temperature is about 45°C. (*e*) Salts and Cl ions are essential for *its action.* (*f*) *Amylase is not present in the pancreatic juice of infants up to the age of about* 6 *months.* Hence, during this period the baby should not be given any starchy food.

Stages of action of pancreatic amylase are same as that of ptyalin. All starch and dextrins when exhaustively acted both by salivary and pancreatic amylase successively are converted into maltose, dextrin and isomaltose. The latter two are not hydrolysed to maltose and ultimately glucose due to the absence of oligo-α-1, 6′ glucosidase and appreciable amount of maltase in either saliva or pancreatic juice. After this, digestion by intestinal juice begins.

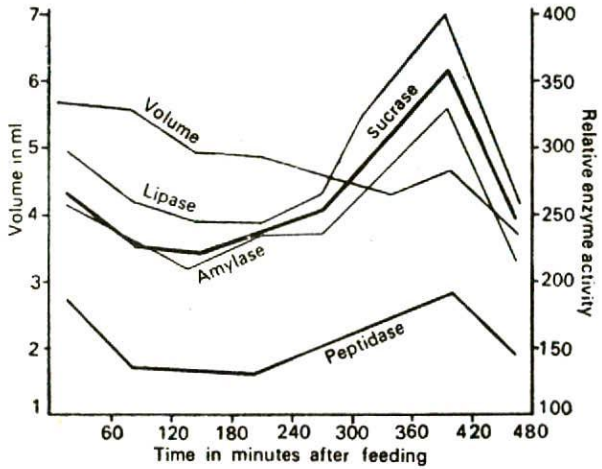


FIG. 347. Graphical tracing representing average secretion of succus entericus (intestinal juice) from isolated jejunal loop.

In the succus entericus. Succus entericus contains oligo-α-1, 6′ glucosidase which splits α-1, 6′ linkages of dextrin formed by the action of α-amylase thus providing scope of further activity of α-amylose and of isomaltose converting it to glucose. It also contains maltase which hydrolyses maltose to glucose. So the starch is completely hydrolysed to glucose by joint action of α-1, 4′ amylase present in saliva and pancreatic juice and α-1, 6′ glucosidase and maltase in the succus entericus. The other disaccharides taken in food are hydrolysed by lactase and ucrase (invertase) present in this juice. The enzymes, and their substrates pon which they act, and the respective end products are given below:

1. **Sucrase (invertase)**—acts on sucrose producing 1 molecule of *fructose* and 1 molecule of *glucose*.
2. **Lactase**—acts on lactose giving 1 molecule of *glucose* and 1 molecule of *galactose*.
3. **Oligo-1, 6′ glucosidase**—converts isomaltose into glucose and splits α-1, 6′ linkages of dextrin.
4. **Maltase**—acts on maltose giving *two glucose molecules*.

(It has been suggested that there are more than one kind of *sucrase*, lactase or maltase).

5. **Amylase**—traces of this enzyme may be present in the succus entericus. The presence of this enzyme at a low concentration has been established. It is supposed to act on that little quantity of starch and dextrin which might have escaped pancreatic digestion.

Evidences indicate that *many or all intestinal enzymes are intracellular. Their presence in the juice is due to cell desquamation.*

Thus, the digestible carbohydrates are all converted into monosaccharides in which form they are absorbed. The process of starch digestion is slow and prolonged. So monosaccharides are slowly produced as observed by restricting disaccharides in the diet. Thus their absorption becomes slow and a high rise of blood sugar is prevented. Consequently, *this can be considered as a process for maintaining blood sugar level within a constant range.*

DIGESTION OF PROTEINS

Introduction. Dietary protein is *indispensable* so the adult require 0·5–0·8 gm of protein per Kgm of body weight per day to remain in nitrogen balance and growing children require more, i.e., 4 gm per Kgm of body weight per day. Proteins are absorbed in the form of amino acids. So the proteins are digested to amino acid from prior to their absorption. The protein digestion which takes place in the intestine includes the (*a*) protein contained in the digestive juices (30 gm) and (*b*) protein derived from desquamated cells (25 gm) along with ingested protein.

The **different forms** in which proteins are taken in diet are as follows: (*a*) *Various types of albumins and globulins.* This is the chief form of food protein. (*b*) *Nucleoprotein.* (*c*) *Caseinogen* (of milk). (*d*) *Collagen* and *gelatin.* (*e*) *Mucin.* (*f*) *Elastin.*

Of these proteins, elastin cannot be digested. All the other varieties are broken down up to the stage of amino acids by the *endopeptidases*, e.g., pepsin, trypsin and chymotrypsin and by the *exopeptidases* in the lower part of the intestinal tract. Albumin and globulin being the chief proteins of diet whose digestion will be described in detail. The differential peculiarities of the other forms of proteins will be mentioned separately.

Protein digestion starts in gastric juice and is finished in the succus entericus due to the absence of proteolytic enzyme in saliva. Brief details are as follows:

In the gastric juice. *Pepsin* is the proteolytic enzyme of gastric juice. It acts with the help of HCl and converts all digestible proteins up to the peptone stage. Proteolytic enzymes other than pepsin (e.g., *cathepsin, parapepsins, gastricsin*) with the pH optima from 1·8–4·5 are present in gastric juice. Although gastric digestion of protein is dispensable (since atrophy of gastric mucosa does not interfere nitrogen equilibrium) but in normal functioning of stomach at best 10–15% of protein is broken down to amino

acid in the stomach as evident by the study of the product of gastric digestion of protein of the diet delivered in the intestine which is a mixture of undigested bundles of muscle fibres, a native protein in solution and products of peptic digestion, i.e., from large polypeptide to a few amino acids.

Peculiarities of pepsin and its action. (1) Pepsin is protein in nature. (2) It remains as pepsinogen in the peptic cells of the stomach. HCl of gastric juice converts it into active pepsin. About 15% of the nitrogen content of the pepsinogen molecule is lost during activation. (3) Optimum pH is 2·0, i.e., highly acid. In alkaline or neutral medium it is inactive. (4) Optimum temperature is about 40°C. (5) It attacks the *peptide linkages* of the protein molecules and breaks them at these links. (6) It acts on proteins and digests them up to peptone. After complete peptic digestion about one-tenth of the total number of peptide linkages are broken down. (7) Its action on the living gastric mucous membrane is prevented by the presence of *antipepsin* in the gastric mucosa.

Stages of digestion. Pepsin in presence of HCl digests proteins to peptone (mainly) through the following stages: Protein → acid metaprotein → primary proteoses → secondary proteoses → peptone → amino acid (Fig. 348).

The last component is allowed for absorption and consequently the major part of protein digestion must occur in the intestine by other proteolytic enzymes.

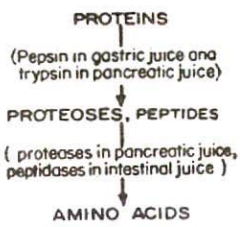


Fig. 348. Schematic diagram showing protein digestion (simplified).

In the pancreatic juice. *Trypsin* is the proteolytic enzyme of pancreatic juice. Its **nature** and **conditions of action** are as follows: (1) *Trypsin is secreted as inactive trypsinogen. It is activated by the action of* **enteropeptidase** (enterokinase) present in the succus entericus. Consequently, until pancreatic juice comes in contact with succus entericus it will possess very little proteolytic activity. Inactive trypsinogen can act on protamines and peptones slightly. *Activation can also be brought about by calcium salts.* (2) *Trypsin is protein in nature.* (3) *Optimum reaction* is slightly on the alkaline side but it can act to a fair extent in a slightly acid medium. Optimum pH varies with the type of protein to be acted upon, viz., for caseinogen and peptone, 8·0; for gelatine, 9·7, etc. (4) *Optimum temperature* is about 40°C. (5) *It can act upon native proteins as well as upon the products of protein digestion*—such as, *metaprotein, proteose, peptones, polypeptides,* etc.,—and converts them all into lower peptides (tri- and dipeptides). Trypsin attacks the peptide linkage. The products formed after the action of pepsin will be cleaved if arginyl or lysyl group. Protamines containing large amount of arginine increase tryptic activity. In prolonged tryptic digestion even some amino acids may be formed, viz., leucine and tyrosine. *This wide range of action is its characteristic feature which is not found with pepsin.*

(1) Inactive pancreatic juice contains two zymogens: (*a*) *trypsinogen,* and (*b*) *chymotrypsinogen.* Enterokinase converts trypsinogen into trypsin and trypsin activates chymotrypsinogen into chymotrypsin. So that when enterokinase is added to inactive pancreatic juice both the zymogens become activated. Trypsin itself can similarly activate trypsinogen into trypsin as a process of **autocatalysis.** Chymotrypsin coagulates milk like

rennin. It also hydrolyses casein and gelatin, but its mode of action is different from trypsin. Both trypsin and chymotrypsin are **endopeptidases.** (2) Further breakdown of proteins is carried out by the **exopeptidases,** e.g., (*a*) *aminopeptidase,* (*b*) *carboxypeptidase,* (*c*) *tripeptidase* and (*d*) *dipeptidase.* These enzymes act upon different fractions of the digested protein molecule. Aminopeptidase splits off those amino acids from the polypeptide molecule which possess a free amino group. Similarly, carboxypeptidase takes away those ones which possess a free carboxyl group. Tripeptidase and dipeptidase split off tri- and dipeptides to amino acids. Pancreatic juice also contains two other protein-splitting enzymes namely **elastase** and **collagenase.**

Stages of breakdown. Stages of tryptic activity are as follows:

Proteins→ alkali metaproteins→ primary proteoses→ secondary proteoses→ peptones→ polypeptides→ lower peptides→ amino acids. 50–60% of proteins is digested in the pancreatic juice. Here, tryptic digestion ends and erepsin action begins.

In the succus entericus. Digestion of protein in the intestinal juice depends upon the tryptic activity as the proteolytic enzyme present in the intestinal juice is unable to hydrolyse the protein as such. Removal of protease results loss of 50% protein in the stool which may be checked by the introduction of pancreatic trypsin. **Erepsin** consists of a mixture of enzymes (intracellular) including *aminopeptidases* and *dipeptidases.* Its **nature** and **conditions of action** are as follows: (1) It acts best in slightly alkaline medium, **optimum pH** is about 8·0. (2) *It cannot act on native proteins. It acts only upon lower peptides and converts them completely into amino acids.* (3) It is not a pure entity. It consists of many different peptidases. The various peptidases act serially, one after the other, upon the smaller and smaller fragments of the peptide molecule, till they are completely broken down into amino acids. At each stage of digestion a different peptidase comes into action. The epithelium of the intestine is very rich in these peptidases. From this it is suggested that the digestion of lower peptides may take place partly inside the epithelial cells during absorption.

Thus the proteins are converted into amino acids, and are absorbed.

DIGESTION OF NUCLEOPROTEINS

The proteolytic enzymes, pepsin and trypsin, hydrolyse nucleoproteins into their protein and prosthetic part nucleic acid components, in the first step. The former is digested as outlined in protein digestion. The nucleic acids are depolymerised by the hydrolytic action of pancreatic *ribonuclease* and *deoxyribonuclease* with the production of **oligonucleotides** and certain pyrimidine **mononucleotides.** The former are converted to *mononucleotides* by intestinal *phosphodiesterases.* The mononucleotides are hydrolised by non-specific phosphatases yielding nucleosides and inorganic phosphate.

The different stages of digestion of nucleoproteins (Fig. 349) which takes place in the intestinal mucosal cells mainly are summarised in the scheme as on p. 504.

Digestion in the intestine takes place partly in the lumen by succus entericus, containing enzyme derived from desquamated cells and mainly in the epithelium of the gut, because, the enzymes are concentrated in

the epithelial cells. It is believed that the *two pyrimidine nucleosides are not hydrolysed further and are absorbed as such.*

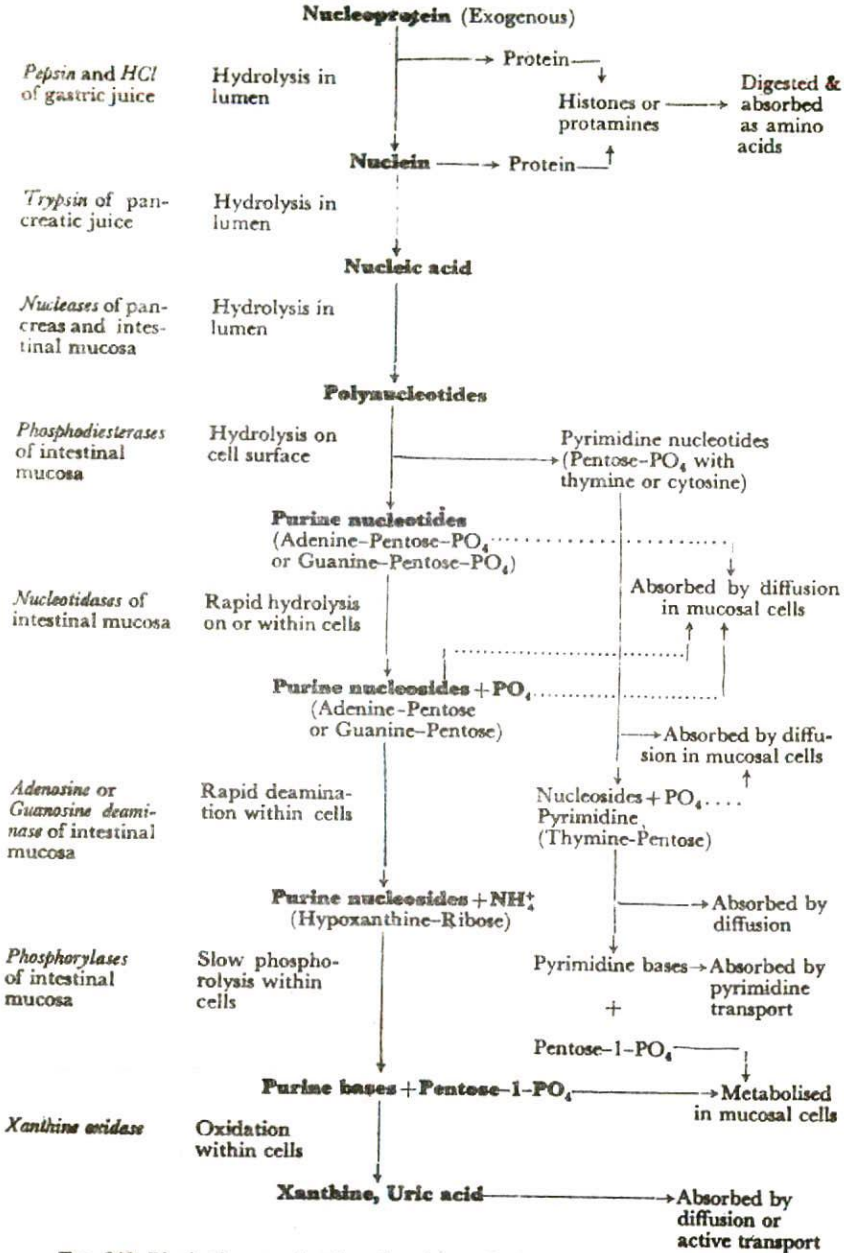


FIG. 349. Block diagram showing digestion and absorption of nucleoproteins.

DIGESTION OF CASEIN

The chief protein of milk is casein, a complex phosphoprotein. The fourth stomach of ruminants contains a protein-splitting enzyme rennin which causes clotting of milk. It liberates paracasein from casein which is precipitated as calcium paracaseinate. Although rennin is absent in human stomach, but **chymosin** is present in infant's stomach which does the same action of rennin of ruminants. Chymosin is distinct from pepsin and absent in adults. Other proteases present in the stomach can convert casein to paracasein. Tryptic and chymotryptic digestions convert it to phosphopeptones containing phosphoserine.

Digestion of milk. Three constituents of milk require digestion: (1) Protein—(*a*) *Caseinogen*—Its digestion has been described above. (*b*) *Lactalbumin* and *Lactglobulin*—They are digested in the same way as proteins—successively by pepsin, trypsin and erepsin. (2) *Fats*—They undergo the same process of digestion as other fats. (3) *Lactose*—digested by lactase to glucose and galactose.

Digestion of collagen and gelatin. Collagen is present in white fibrous tissue, tendons, bones, etc. Gelatin is prepared from it by boiling with acid. Its digestion proceeds as follows: *In the gastric juice: Collagen→ →gelatin→gelatoses→gelatin peptone.* Pancreatic juice digests this peptone up to polypeptide which in its turn is digested by succus entericus up to amino acids.

Digestion of mucin. It is a glucoprotein. Gastric juice breaks it into glucosamine and another peptone-like substance. The latter is further digested as other peptones. Glucosamine is probably absorbed as such.

DIGESTION OF LIPIDS

Different forms of lipids taken in diet are (1) neutral fats, (2) phospholipids, (3) cholesterides, (4) free cholesterol, (5) fatty acids, and glycerol (Fig. 350). The last two groups do not require any digestion, because they are absorbed as such. The first three groups are digested in the alimentary canal.

Neutral fats are digested into fatty acid and glycerol. Hydrolysis of fats takes place in stages. In the first stage there is formation of one molecule of fatty acid and a diglyceride. The diglyceride is broken down into another molecule of fatty acid and a monoglyceride. The monoglyceride is finally hydrolysed into another molecule of fatty acid and glycerol. So the fat molecule after complete hydrolysis gives rise to 3 molecules of fatty acids and 1 molecule of glycerol. All other fats are digested in similar manner but their end products are different. Saliva does not contain any lipolytic enzyme. Digestion starts in the stomach and ends in the succus entericus. Brief details are as follows:

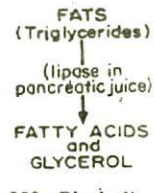


Fig. 350. Block diagram showing fat digestion by lipase, facilitated by emulsion by bile (simplified).

In the gastric juice. Gastric lipase is a distinct lipolytic enzyme present in the gastric juice. Its **characteristics** are as follows: (*a*) It breaks neutral fat into one molecule of glycerol and 3 molecules of fatty acids. (*b*) *It acts best in slightly acid medium, but is destroyed by* 0·02% *HCl in* 15 *minutes.* Hence, its action takes place only in the initial stages of gastric secretion when the acidity

is not high. (*c*) Optimum temperature is about 40°C. (*d*) It acts best on emulsified fat, i.e., egg-yolk, milk, etc. Due to these characteristics gastric lipase is not of much importance. Hydrolysis of fat in stomach is not significant, since most of the ingested fat is found in the duodenum and presence of lipase in the stomach is by way of regurgitation from the small intestine.

In the pancreatic juice. Fat digestion is mainly carried out in the duodenum by **pancreatic lipase** or sometimes called as **steapsin.** According to some, pancreatic lipases are of two different types, one acting on *glycerol esters of lower fatty acids* and the other acting on *glycerol esters of higher fatty acids*. Since fat is insoluble, pancreatic lipase acts on triglycerides in emulsified form in the lumen. Emulsification of fat takes place by bile salts, fatty acids, cholesterol, monoglycerides, lysolecithins and proteins. Fatty acids and monoglycerides pass into micellar phase with bile salts and they in this way are made water-soluble. Fat digestion is nearly completed by the pancreatic juice. This is due to the fact that not only pancreatic lipase, but several other factors also help in the process. The factors that help lipase in its action are as follows: (1) Bile salts help fat digestion in a number of ways (*vide* pages 446–47). (2) Presence of antiperistalsis in the duodenum is of considerable importance in this respect. It helps thorough admixture and keeps fatty food for a longer time in the duodenum, to ensure maximum digestion. (3) Pancreatic lipase acts best in a slightly alkaline medium (pH 8·0). The alkalinity of the pancreatic juice and bile helps to maintain a suitable reaction and facilitates lipase action. (4) Presence of fats in the duodenum liberates *enterogastrone* which inhibits gastric secretion and motility. Thus, emptying of stomach is delayed. *Fats also stimulate bile secretion as well as bile expulsion.* Thus fatty food adapts the environment in such a way that its own digestion is facilitated. (5) Amino acids like *arginine, histidine* and *lysine* also help in the hydrolysis of fat. **Phospholipases, cholesterol esterases**—These are other enzymes of pancreatic juice acting on other lipids for their digestion. The former removes one fatty acid from lecithin and cephalins yielding substances called **lysolecithins** and **lysocephalins.** These are acted upon by phospholipases B, which removes the second fatty acid yielding glycerol-phosphoryl-choline and other similar compounds. Glycerol is split off by phosphodiesterase, and the base choline and sphingosine, etc., are subsequently freed by the action of phosphatases. Cholesterol is freed from cholesterides by cholesterol esterase.

In the succus entericus. Succus entericus also contains another **lipase.** Since under normal condition fat digestion is almost completed by pancreatic juice, this lipase is of little importance. It is needed only to deal with that little quantity of fat which might have accidentally escaped pancreatic digestion.

Isotopic studies indicate that fat hydrolysis is faster than fatty acid absorption.

Synthesis of triglycerides and recombination of fatty acids in different OH groups of glycerol take place in lumen. Hydrolysis of short-chain triglycerides takes place by lipase in the mucosae of the intestinal epithelium.

Pancreatic lipase hydrolyses triglycerides to fatty acids and 2-monoglycerides. The latter is not hydrolysed further by pancreatic lipase, 2-monoglycerides converted to 1-monoglycerides and hydrolysed by pancreatic

lipase to fatty acids. Recombination also occurs in diglycerides and triglycerides and a labelled fatty acid found to be distributed between one and three position and not in two position by the action of pancreatic lipase.

(2-monoglycerides are hydrolysed with mucosal cells which contain a different lipase distinct from pancreatic lipase. Triglycerides of short-chain (trioctanoin) are hydrolysed by this enzyme and triglycerides of long-chain (tripalmitin) are not. Fats are immisible with H_2O and most artificial or natural emulsions are broken within the stomach.)

ABSORPTION

Definition. Absorption *is the process by which the end products of digestion pass through the intestinal epithelium and enter the blood stream.*

General principles of absorption

Attempts have been made to explain the mechanism of absorption on the basis of known physico-chemical principles. The following factors are believed to be involved in the process:

1. **Diffusion.** This depends upon the relative concentration of the substances on either side of a permeable membrane. The concentration of the end products of digestion is much higher in the intestine than in blood in health. This difference initiates diffusion currents from the lumen of the intestine into the blood stream and thus helps absorption.

2. **Hydrostatic pressure.** Hamburger found that amount of absorption is directly proportional to the hydrostatic pressure in the intestine. The intestinal contents at the height of digestion exerts considerable pressure which is all the more enhanced by the tone and movement of the intestine. This higher pressure causes filtration of water and dissolved substances across intestinal epithelium.

3. **Osmotic pressure.** The colloidal osmotic pressure in the capillary loop of the villus is fairly high and is nearly two to three times higher than the blood pressure existing in it. This high osmotic pressure helps in drawing the fluid from the lumen into blood. [It should be noted that the same factors help in absorbing water and metabolites from the tissues into the venous side of the capillaries.]

4. **Adsorption.** This process is also involved in the absorption of certain substances. It is a very subtle process of union by which a particular substance while being absorbed from the intestine can carry another substance along with it.

5. **Hydrotropy.** This is a process by means of which substances insoluble in water are converted into soluble forms. In this way they are brought into a suitable state for absorption. This action is effected by bile salts upon fatty acids and similar products.

6. **Electrical effects.** Heber has suggested that a process of cataphoresis (the transfer of a solute across a membrane from anode to cathode) may be set up during absorption and may be of considerable importance in this respect. The **cations** will move towards the side with a *negative potential charge* and the **anions** towards the *positive potential charge*. In addition to this electrical phenomenon the fluid will exert effect on the solute particles. This is known as **solvent drag phenomenon.**

7. **Passive and Active transport.** In the passive transport mechanism, special physical force is not required. As for instance if any particular food substance remains in higher concentraion in the lumen of the intestine

the energy for movement is derived from the higher concentration of the food substance.

In the active transport mechanism, there is a carrier mechanism which helps in movement of the food substance against the electrical forces. ATP supplies energy to this **carrier system.**

8. **Chemical action.** In many cases it is seen that brisk chemical action goes on inside the cells of the epithelium during absorption.

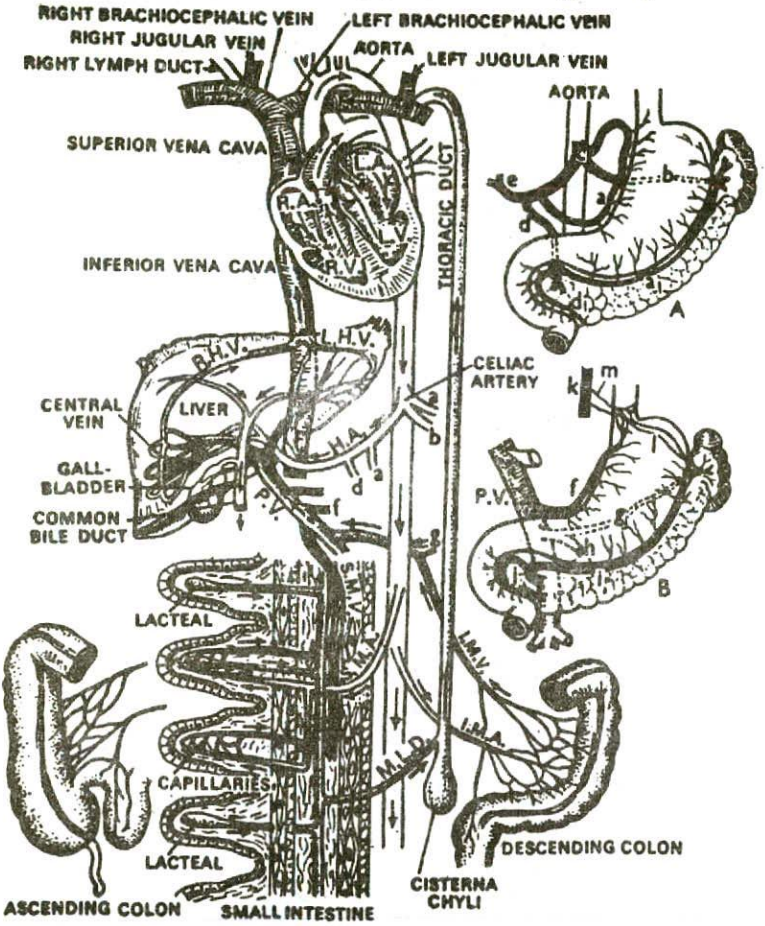


FIG 351. Diagram representing absorption with inset A showing arterial supply of and inset B, venous supply of stomach.

R.H.V.—right hepatic vein, L.H.V.—left hepatic vein. H.A.—hepatic artery. P.V.—portal vein. S.M.V.—superior mesenteric vein. S.M.A.—superior mesenteric artery. I.M.V.—inferior mesenteric vein. I.M.A.—inferior mesenteric artery. M.L.D.—mesenteric lymph duct. *a*—gastric artery. *b*—splenic artery. *c*—celiac artery. *d*—gastroduodenal artery. *e*—hepatic artery. a_1—gastro-epiploic artery. d_1—pancreaticoduodenal artery. *f*—gastric vein. *g*—splenic vein. *h*—inferior mesenteric vein. *i*—gastro-epiploic vein. *j*—pancreaticoduodenal vein. *k*—azygos vein. *l*—short gastric vein. *m*—oesophageal vein. R.A.—right auricle. L.A.—left auricle. R.V.—right ventricle. L.V.—left ventricle.

Although it is certain that some of the above processes are essentially involved in the phenomenon of absorption, yet, there are certain aspects of the process which cannot be explained on these principles only. For instance, the rapidity of absorption, the selective absorption of certain substances, the absorption of glucose and NaCl from hypotonic solutions and many other similar phenomenon cannot be explained in this way. This shows that in addition to this, some other forces are also at work.

It has been shown that the epithelial covering of the villus is not a passive membrane, submitting itself to physical forces only (like Bowman's capsule of the nephron), but intense chemical activity goes on inside the epithelium during active absorption. This is proved by the fact that absorption entails a good deal of oxygen consumption and expenditure of energy on the part of the absorbing epithelium. Moreover, when the temperature of a loop of intestine is reduced to 0°C., preferential absorption of glucose ceases altogether. *All these facts show that besides physical forces, some form of chemical activity is certainly and essentially involved in the process of absorption.*

The **interrelation between digestion and absorption** should also be noted in this connection. It is true that an adequate digestion is essential for absorption, and as a matter of fact, the whole digestive machinery has evolved with the only intention of making the foodstuff suitable for absorption. But if we look to the phenomenon from the opposite standpoint, it will be seen that absorption also is no less important for digestive process. The two processes—digestion and absorption—are closely, interdependent. One cannot go without the other. The following considerations will clarify: (1) As digestion proceeds the number of discrete particles increase and unless they are removed by absorption, the osmotic pressure of the medium will rise, a considerable amount of water will be drawn out from the surrounding tissues, thus upsetting the very purpose of digestion altogether. But since, absorption does take place, no such osmotic disturbance occurs at all. (2) Absorption helps digestion also in another way. It is known that the action of the digestive enzymes is reversible. So that unless the end products are quickly removed they will accumulate and after a time reversible action will be set up by which the digested particles will again be synthesised. In this way the rate of digestion will come to a standstill with the establishment of a dynamic equilibrium. Absorption removes the end products, prevents the reversible process and thereby helps to make digestion complete.

One feature of **histological interest** is also to be noted in this connection. The cells of the absorbing epithelium are found to be longitudinally striated in their free border. This type of *brush border epithelium* is also found in other places whose chief function is absorption, for instance the renal proximal tubules. Examination under electron microscope reveals that the brush border is actually minute villi like projections, named *microvilli*. This increases the effective absorbing surface of the villi to a great extent.

Stomach absorbs very little food because, under normal conditions, the end products of gastric digestion are not absorbable. For this reason gastric mucosa has not been adapted for absorption and therefore contains no villi. But those simple substances which do not require digestion at all, may pass through the gastric epithelium. Hence water, alcohol, saline, glucose and certain easily diffusible drugs are absorbed by stomach to some extent.

Small intestine *is the chief place for absorption* (FIG. 352). Its upper part is more concerned with secretion, whereas, the lower part for absorption. The end products of digestion as well as salts, vitamins and water—are all absorbed through small intestine. The enormous length of the small intestine affords a large surface area for maximum possible digestion and absorption. *The villi of the small intestine are the absorbing units.* They are more numerous in the lower parts than in the upper. *There are about* 5,000,000 *villi in the human intestine with a total absorbing area of nearly* 10 *sq. metres. The end products of protein and carbohydrate digestion are absorbed by the vascular capillaries in the villi and are then drained into the portal system. But the fats mainly pass through the lacteals of the villi and are then carried by the lymphatics.* The nature of the factors which determine different routes of absorption for the different foodstuffs, is not known.

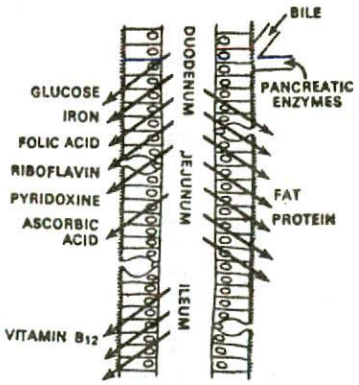


FIG. 352. Schematic representation of sites of absorption of various substances in the small intestine (diagrammatic).

Large intestine *mainly absorbs water.* Saline, glucose alcohol, and certain drugs may to some extent be also absorbed from this part.

Although large amount of water is absorbed from the small intestine, yet, it cannot be complete, because a watery medium must be maintained in this part to facilitate digestion and absorption of foodstuffs. But when the chyme reaches the large intestine, it seldom carries any undigested and unabsorbed foodstuff. Consequently, a watery medium is no more necessary. For this reason all the water is absorbed producing what is known as the 'formed' stool. This water absorption reduces bacterial putrefaction by making the medium dry and is also very useful in conserving the water content of the body.

ABSORPTION OF CARBOHYDRATES

End products of carbohydrate digestion are all monosaccharides, such as glucose, laevulose, galactose, xylose, mannose, arabinose, etc. It is in this form that carbohydrates are absorbed. It is believed that little quantities of disaccharides may also be absorbed, but the still higher forms are not absorbed at all.

Mechanism of absorption. The monosaccharides being highly soluble in water, the physical forces like osmosis, diffusion, filtration, etc., certainly play a considerable part in their absorption. But if these were the only forces concerned in the process, the rate of absorption should have been directly proportional to their concentration in the gut. But this linear relation is found to hold only in the cases of xylose, arabinose, and mannose. With other sugars this principle does not apply; for instance, *the amount of glucose and galactose absorbed per hour is entirely independent of their concentrations in the gut.* Laevulose occupies an intermediate position. Moreover, *the rate of absorption varies with the nature of sugars.* If the rate of **glucose** absorption is taken as the standard (i.e., **100%**), then **galactose** is found to be absorbed much more rapidly (**115%**); whereas the rate of absorption

of **laevulose** is about half that of glucose (i.e., **44%**); of **mannose** (**33%**) and **xylose** (**30%**) is about one-third that of glucose. Other sugars are still more slowly absorbed. Hydroxyl group at position 2 of the sugar molecule seems to be essential for their active transport. It is found that when the temperature of the mucous membrane is brought down between 0°C. to 20°C., the difference in the rates of absorption between glucose, galactose, laevulose and other sugars disappears. Under such conditions, they are all absorbed slowly, but at the same rate.

These observations indicate that the preferential treatment done towards glucose, galactose and laevulose is due to some chemical activity going on inside the cells. Phloridzin (phlorrhizin) or iodo-acetic acid retards the high rate of glucose and galactose absorption. Since, these substances paralyse the activity of phosphatase it is probable that this enzyme is intimately concerned with the process. *Verzer has suggested that during absorption, phosphorylation of sugars takes place* and the corresponding hexose phosphates are formed. The formation of these compounds keeps down the concentration of free glucose, etc., in the cells and thereby ensures their rapid absorption. In this way the high rate of absorption of these sugars can be explained. It is almost certain that on the other side of the epithelial cells a reversible reaction takes place (dephosphorylation) in which the hexose phosphate is broken down, free glucose enters the blood stream and the phosphoric acid is retained in the cells for further phosphorylation. It is interesting to note that the same mechanism also takes place in the reabsorption of glucose by the renal tubules.

Thus from the above it can be concluded that in addition to the physical forces the following factors are necessary for rapid absorption of sugars: (1) *Complete digestion* into monosaccharides, (2) *presence of phosphoric acid and phosphokinase* enzyme in the epithelial cells, (3) *adrenal cortex* and *insulin* which probably control the process of phosphorylation, (4) *anterior pituitary*—whose exact role is not known, but which may act indirectly through adrenal cortex, (5) *sodium salts* also exert some effects. Because in adrenalectomised animals the rate of absorption of glucose can be restored to normal by giving sodium salts. (6) *Vitamins*—Thiamine, pantothenic acid and pyridoxine may help in the process of absorption. (7) Blood glucose level has got no effect on absorption of glucose.

Pathway of absorption. Carbohydrates are almost completely absorbed *through the portal system*, because portal blood always shows a higher concentration of sugars during absorption. An inconspicuous amount may pass through the lymphatics.

Site of absorption. Glucose is maximally absorbed in jejunum.

ABSORPTION OF PROTEINS

Forms in which proteins are absorbed (FIG. 353). I. *Dietary proteins under physiological conditions are absorbed as amino acids*, which are the end products of digestion.

II. Small amounts of peptides may also be absorbed from the alimentary canal. This is proved by the following observations: (*a*) Small amounts of unchanged proteins, proteoses, peptones, polypeptides may be absorbed. (*b*) Serum proteins and raw egg-whites can also be absorbed to a small extent. (*c*) Some people are very sensitive to shell fish, crab, prawns, strawberries and such other articles of food. Even hypersensitiveness to milk has

been reported. Such cases of dietary idiosyncrasies indicate that proteins of these substances are absorbed to some extent in unchanged form. These foreign proteins entering circulation stimulate the production of antibodies and the antigen-antibody reaction is responsible for *allergic symptoms*. (*d*) One more curious fact is that if an animal's own serum be introduced into a loop of intestine (washed clean of any trace of proteolytic enzyme) the whole of the serum is absorbed in unchanged form.

From the above it will be noted that proteins, higher than amino acids, can be absorbed to some extent. In infants the cellular lining of the alimentary canal, being delicate, is more permeable to these higher forms. Moreover, in unhealthy conditions of the alimentary tract, such as diarrhoea, dysentery, etc.,—where the mucous membrane is ulcerated,—these foreign proteins may be absorbed in greater amounts and may cause various disturbances in the body. These foreign proteins generally pass out unchanged.

However, under physiological conditions, proteins are absorbed in the form of amino acids only. Absorption of amino acids might be either an active or a passive process. D-isomers which are less rapidly absorbed are carried by passive diffusion whereas the more rapidly absorbed L-isomers

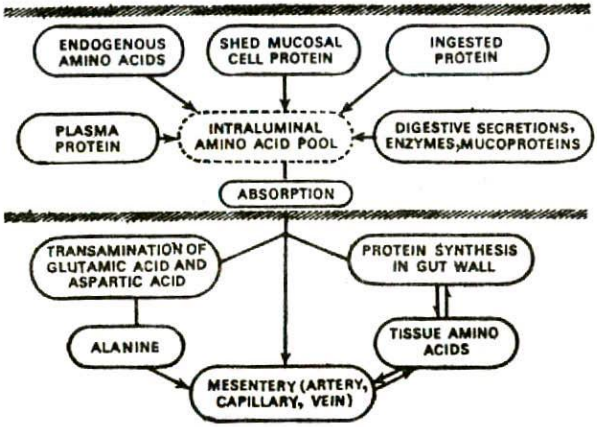


FIG. 353. Block diagram showing origin and deposition of amino acid pool in the small intestine.

are actively transported. It has also been observed that there are separate transport mechanisms for neutral and basic amino acids and also for *proline* and *hydroxyproline*. Vitamin B_6 and Mn^{++} have some roles in the process of concentration of amino acids, by the cell; deficiency of the vitamin affects the intestinal transport of amino acids. Na concentration gradient from lumen to cell also accelerates amino acid absorption.

Regarding the **pathway of absorption,** they pass chiefly through the portal system. Negligible amount may enter the lymphatics. The blood of fasting animals *contains* 3–6 mgm of amino acid nitrogen per 100 ml. After meal the amount rises to 8–10 mgm.

Transamination during protein absorption. To keep a balance between the amino acids obtained from dietary source and those required

in the body, it has been suggested that the intestinal mucous membrane can, to some extent, transform one amino acid to other.

ABSORPTION OF FATS

The absorption of fat is perhaps considered to be the most complicated mechanism in tne subject of biochemistry. In the past, two theories regarding fat absorption mechanisms were advanced by Pfluger, Verzer and McDougall (known as **lipolytic hypothesis**) and Frazer (known as **partition hypothesis**) but recent studies have thrown more light on this mechanism.

1. **Lipolytic hypothesis** or **theory of Pfluger, Verzer and McDougall.** Triglycerides (fats) are absorbed mainly in the lymphatics after they have been resynthesised from fatty acid and glycerol in the mucosal epithelial cells. The fatty acid and glycerol are derived from hydrolysis of ingested fat (after emulsification) by *lipase* in the lumen. Negligible amount of fatty acid is absorbed in the portal vein as **fatty acid bile salt complex.**

2. **Partition hypothesis of Frazer.** Fats are absorbed partly (*a*) in emulsified form (without hydrolysis) into the lymphatic channel and pass into the blood through the thoracic duct, and partly (*b*) in the form of fatty acid bile salt complex into the portal vein, the fatty acid derived from the hydrolysis of fat by lipase in the intestinal lumen. Evidences indicate that the neutral fat is found to be absorbed in spite of hydrolysis being interfered by the addition of sodium acetylsulphate in the lumen and emulsified fat is absorbed even after ligation of pancreatic duct. This theory holds that the fat is not resynthesised in epithelial cells.

Very recent studies on this subject have thrown a considerable light in unfolding the intricate mechanism of fat absorption. The recent knowledge regarding the mechanism of fat absorption has been briefly discussed below:

Most dietary fat of either vegetable or animal origin comprises of triglycerides in which glycerol is combined in low-energy ester linkages with three fatty acids and the fatty acids are of even number of carbon atoms. Fatty acids are both saturated and unsaturated which are almost entirely palmitic and stearic in case of former and in case of the latter oleic and linoleic acids. These are **long-chain fatty acids.** Milk fat contains 3–10% (C_4–C_{14} acids) contributing **shorter-chain fatty acids.**

Since fats are insoluble in water and immiscible in chyme, so fat neither is absorbed as such nor is digested by *lipase* (due to lack of contact with lipase) to fatty acid and glycerol for absorption. Emulsification of fat by different emulsifying agent is required for preparing it suitable for both digestion and absorption and this process (emulsification) possible in small intestine where bile salt and other agents are present. Bile salts themselves are relatively weaker than the mixture of bile salts and a polar body—*lecithin*, *lysolecithin* or *monoglycerides* as emulsifying agent. The latter two are produced by the action of pancreatic lipase on lecithin or triglycerides. Thus the enzymic action tends to stabilise the emulsion.

So fat digestion and absorption do not occur in stomach significantly which is devoid of emulsifying agent but natural (milk fat) or artificial emulsions are digested in the stomach.

Recent studies account for many aspects of fat absorption better than previous supposition.

It has been observed that (1) fatty acid is absorbed more readily than any other components, i.e., triglycerides, 1-monoglycerides, 2-monoglycerides, diglycerides and free fatty acids (which are formed in the sample collected near the duodeno-jejunal junction) and (2) the hydrolysis occurring in the lumen is faster than the absorption of free fatty acid. (3) There is spontaneous migration of fatty acids from one alcohol group to another in the glycerol.

The chief products of luminal hydrolysis of triglycerides are 2-monoglycerides and free fatty acid. Glycerol and 1-monoglycerides are quantitatively less important while fat is undergoing digestion and absorption. The fat is distributed among the emulsified fat droplets, micells (small), hydrated polymolecular aggregates and molecular solution. Micells of intestine contain three major components as bile salts, monoglycerides and fatty acids.

The salts spontaneously aggregate with monoglycerides and form micells when the concentration of bile salts attains a certain value known as *critical micellar concentration*. Since the concentration of conjugated bile salts remains always higher than the critical micellar concentration (at ordinary circumstances), the monoglycerides rapidly form micells as soon as they are liberated from triglycerides by lipase actively with bile salt.

As the micell once formed it dissolves free fatty acid, cholesterol and fat-soluble vitamins and dissolution varies directly up to a limit with the amount of monoglyceride contained in it. But the unconjugated bile salt has got *higher critical micellar concentration* for which fat absorption is inhibited when bile salts are deconjugated in the gut. The inhibition of absorption of fat (due to deconjugation) is for the inability of micellar solution at this condition of holding monoglycerides and free fatty acids liberated from lypolysis and thereby these are precipitated and become unavailable for absorption.

Lipid molecules in solution can diffuse into the epithelial cells through its lipoprotein membrane. So the metabolic machinery contained in the endoplasmic reticulum of the cell takes up monoglycerides and free fatty acid and rapidly synthesises them into triglycerides. Diffusion gradient from lumen to cell down which free fatty acid and monoglycerides flow is present till the completion of absorption.

The gradient is produced by immediate replacement of monoglycerides and free fatty acids in the solution from the micellar phase as they leave the luminal solution and consequently the luminal solution remains saturated with free fatty acid and monoglycerides. Of the fat digestion products, the monoglycerides and fatty acids are separated from micells to be absorbed in the duodenum and jejunum and conjugated bile salts only in the terminal ileum. The bile salts being insoluble in the cell membrane (due to their charge) must be actively transported. The rate of their absorption is proportional to their solubility and hence the more soluble monoglycerides are absorbed first and then follow other substances in the order of their solubility, viz., long-chain fatty acid, cholesterol, short- and medium-chain fatty acids. And the triglycerides of these acids are absorbed without passing through the micellar phase since they are relatively soluble in solution as well as in the cell membrane. Fat aggregation does not take place in the space between the microvilli and endoplasmic reticulum when fat resynthesis occurs. Lysolecithin enters into the mucosal cell as such and its base is separated there by phosphodiesterase and its fatty acid by lysophosphatidase and finally glycerol and phosphate are separated by non-specific phosphatase.

Within the cells the monoglycerides without further hydrolysis (of long-chain fatty acid) are resynthesised to triglycerides or phospholipids. The shorter-chain fatty acid ester is hydrolised by lipase (intracellular) and not those of long-chain fatty acids (i.e., dietary fat). Mucosal cells can synthesise long-chain fatty acid, i.e., stearic acid (C_{18}) from acetic acid as well as palmitic acid (C_{16}) to stearic acid (C_{18}) with acetic acid.

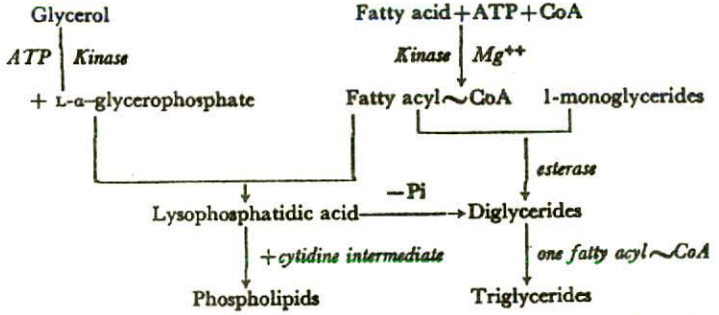


FIG. 354. Schematic representation of the path of synthesis of fat (triglycerides, phospholipids) in the mucosa. *Vide* also FIG. 355.

Glycerol liberated in the lumen by hydrolysis of triglycerides is partly oxidised in mucosal cell to CO_2 and partly goes to liver for its conversion to glycogen and remaining is utilised in the resynthesis of triglycerides. The glycerol required for the resynthesis of triglycerides is also derived from glucose (glycolytic path). Resynthesised fat is absorbed into the lymph.

Intracellular fat transport. After resynthesis, the fat are accumulated more in the apical cells of the tip of villi than at the sides and they are restricted in the supranuclear part of the cell. It appears first as discrete particles in the endoplasmic reticulum. Microsomes derived from the reticulum contain enzymes which resynthesise triglycerides. So fat is seen to be deposited in the reticulum. Resynthesis and absorption take place simultaneously. The entire reticulum is filled with fat droplets and then the fat moves to the supranuclear part of the cell acquiring along its way an envelope of phospolipid and protein and finally they are expelled from the sides of the cell at or below the level of the nucleus.

Chylomicron. Droplets of fat known as chylomicron is formed (aggregation of fat molecules) before the delivery of resynthesised fat into lymph.

The droplets are enclosed in a membrane, composed of small amount of protein, free cholesterol and saturated triglycerides in a monolayer of phospholipid. The fat in the chylomicron reflects the composition of ingested fat (dietary) partly since long-chain fatty acids of the dietary fat are added to mucosal cells for resynthesis whereas most of short- and medium-chain fatty acids and some glycerol are shunted to portal blood. Water-soluble components of fat diffuse into capillaries of the villi which are fenestrated. The gap in the fenestra formed by an uninterrupted basement membrane envelopes the endothelium and the fenestrae are the possible gateway for entry of water-soluble compounds into the capillary blood.

Chylomicron cannot enter the fenestrae due to its particle size. It enters the lacteals through open channels existing between interstitial spaces and the lymphatic lumen. Although the endothelial wall of lacteals is relatively thick but there is absence of enveloping basement membrane

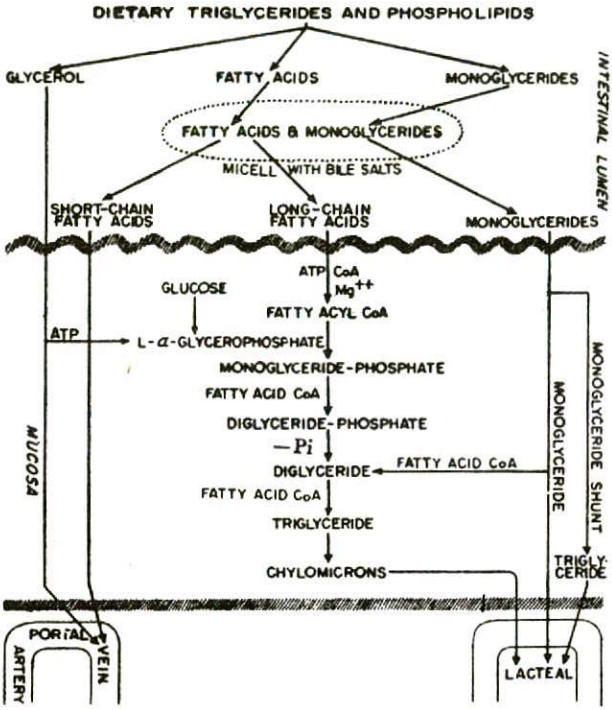


FIG. 355. Schematic representation of the process of absorption of fats (pathway of phospholipids are not shown).

and presence of intercellular space. The fat droplets pass through these spaces. (The cells forming the walls of the lacteal contains many vesicles which may be capable of carrying fat droplets across them due to their pinocytotic property.)

WATER ABSORPTION

Very little water is absorbed from the stomach. Water introduced into the stomach almost immediately passes into the *small intestine which is the chief seat of water absorption.* The intestinal contents near the ileocaecal valve contain the same proportion of water as the upper part of jejunum. But their absolute amount is much smaller. *The large intestine absorbs all the residual water and forms solid stool.*

Absorption of water is not influenced by total water content of the body. There is no limit to the amount of water absorbed. Large quantities of fluid may be ingested without developing liquid stool, showing complete absorption. If more water is taken, more

will be excreted through the kidney. If less is taken, thirst will appear. So that absorption depends upon intake, whereas intake is guided by the water content of the body.

The main physico-chemical forces which help water absorption are **hydrostatic pressure, endosmosis** and **osmotic pressure.** Although the hydrostatic pressure and endosmosis do not play any significant part but the osmotic pressure plays an important role in the *absorption process.* It is interesting to note that water absorption is influenced by the *presence of salts* in it. Pure distilled water is absorbed only up to 59%, but if given in the form of increasing strengths of saline the rate of absorption gradually rises and becomes 95% with a solution containing 0·4–0·7% NaCl. But beyond that strength the rate falls, because, increased osmotic pressure draws out fluid from the wall. It is also to be noted here that, along with water, salts are also absorbed. It is known that for the excretion of salts through the kidney a minimum volume of water is required. So it is reasonable to think that for the absorption of salts from the intestine a minimum volume of water is also necessary. Probably this principle will explain why more water is absorbed in presence of salts. Water and salts are absorbed passively and actively. During **passive absorption,** water and small water-soluble substances traverse the intestinal mucosa along osmotic or electrochemical gradient, the energy moving them being derived from whatever processes established the gradients in the first place. Besides this, water and sodium can also be absorbed against osmotic and electrochemical gradient (active transport). The mechanism is still not known.

ABSORPTION OF SALTS

Stomach and large intestine absorb a little amount, but *small intestine is the main site for salt absorption.* Salts are chiefly absorbed through the blood stream of the portal system. Salts vary in their rate of absorption. Wallace and Cushny have divided the salts into *four main groups according to their rate of absorption:* (1) Sodium chloride, bromide, iodide, formate, acetate, propionate, butyrate, valerianate, caprate. (2) Nitrate, lactate, salicylate, etc. (3) Sulphate, phosphate, ferrocyanide, caprylate, malonate, succinate, malate, citrate, tartrate. (4) Oxalate and fluoride.

The first group is most rapidly absorbed and the fourth group is not absorbed at all. Moreover, the members of the third and fourth groups—all form insoluble compounds with calcium. This may be one of the reasons for their slow rate of absorption.

Although salt absorption depends upon physical factors, yet it is probable that the intestinal epithelium has some power of differential absorption. The salts are selectively absorbed according to their degree of requirement by the body.

Experimental evidence indicates that the intestinal epithelium does not behave as a passive membrane during absorption of salts. On the other hand, it performs considerable amount of work. The sodium ions after being absorbed inside the epithelial cells produce an electric potential which helps in the movements of chloride ions. Due to this electric potential, chloride ions may move inside the epithelial cells, against the high osmotic pressure. Calcium is absorbed in presence of vitamin D, protein and lactose. Calcium absorption is effected by an active transport mechanism which uses high-energy phosphate generated by aerobic metabolism. Iron is absorbed in combination with a special protein called **ferritin.** Absorption is promoted by ascorbic acid which keeps it reduced. The duodenum and upper jejunum are the sites of iron absorption. Iron absorption is regulated by the amount of iron stored in the body.

Phosphate ions are absorbed by all segments of the small intestine, but most effectively from the ileum.

FAECES

The chyme derived from the first food intake requires 36 hours for its lidification to be converted into solid residual matter known as **faeces.**

Roughly about 150 gm of solid stool is passed in 24 hours. If vegetable, coarse cereals and cellulose be excluded from the diet, the faeces show a fairly constant composition as follows:

Water—65%.
Solid—35%.
Ash—15% (mainly calcium, phosphates, iron and magnesium).
Ether-soluble substances (fats)—15% (neutral fats, fatty acids, lecithin, cholic acid and coprosterol).
Nitrogen—5% (derived from purine bases,—about 0·11 gm per day).
Desquamated epithelial cells, bacteria, mucus, undigested and unabsorbed food.

The **reaction** of stool is generally **neutral** or **acid,** but may be slightly alkaline. It is composed of (1) food residues, (2) intestinal secretions, (3) bile, (4) leucocytes, (5) bacteria, (6) epithelial cells, and (7) substances excreted through the large intestine. Since, under normal healthy conditions very little food residue is left, *faeces are not derived from any part of the ingested food.* On analysis no soluble carbohydrates, proteins, or their derivatives are found in the faeces. Moreover, animals, in state of complete starvation, form faeces which shows the same composition as that formed after food. This shows that in a healthy man living upon well-balanced diet, *stool is independent of food.*

Bacteria usually constitute about 9 per cent. of the total solids, but it may be as high as 50 per cent. of the total weight of the faeces. The **colour** of the faeces is due to the presence of **stercobilin** derived from the bile pigments—biliverdin and bilirubin and also to bilifuscins.

Biliverdin and **bilirubin** are reduced to urobilinogen in the large intestine. A certain amount of **urobilinogen** is absorbed through the intestinal wall into blood where it passes *via* portal vein to liver. The liver excretes these pigments as a major constituent of bile, a part of which carried to the kidney through general circulation for their excretion through urine. Unabsorbed urobilinogen in the large intestine is converted to stercobilin.

Interference in the flow of bile by obstruction in the bile duct or by a tumour formation results pale appearance of faeces which conclusively indicates that the normal fate of bile pigments is the formation of stercobilin and its excretion through faeces giving its characteristic yellow colour.

The colour also varies somewhat with the character of the diet, being paler on a high milk diet, black after Fe, etc.

The **odour** of the stool is due chiefly to aromatic substances like **indole, skatole,** etc., and also gases like H_2S. Indole and skatole result specifically from the action of bacteria on amino acid tryptophan. Under normal conditions about 500 ml of gas is passed out per day.

If coarse cereals and vegetables be taken, the composition of the faeces does not remain constant. Because, the cellulose, being indigestible, increases the amount of stool. Also various other substances, which remain inside a cellulose covering are also found in the faeces, under such conditions.

In this way the composition varies. However, cellulose serves the important purpose of increasing the bulk of stool and thus stimulating movement of the large intestine.